Maryland
STATE MEDICAL JOURNAL

Medical and Chirurgical Faculty of the State of Maryland

VOLUME 6 *February, 1957* NUMBER 2

EDITORIAL

ARE WE PRACTICING MEDICINE OR SPECIALTIES?

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Many physicians may consider the question too elementary to warrant any thought or an answer. Yet, it is a question that many of us must frequently ask ourselves. Tending toward more and more specialization, and the subdivision of specialties, we may readily tend to viewpoints that are too narrow to observe the entire patient. Obviously, many physicians must limit actual practice to a specialty. Most of their reading and writing pertains to the specialty. They attend chiefly the meetings of their specialty organizations. The maintenance of a broad viewpoint, and continuing familiarity with general medicine may become difficult but it is accomplished by many.

It is clear that the entire patient, including his nervous system, must be covered in a diagnostic survey. If the physician practicing a specialty has not made a complete physical examination, he should be thoroughly acquainted with all of the findings as reported by the other examiners. Only by familiarity with all the findings can one attain a proper perspective.

Although specialties have been practiced for a long time, patients generally expect physicians to be familiar with all ailments of all parts. They do not classify their complaints to fit the various systems and parts of the body. They are unable and unwilling to confine their complaints to a single specialty. As physicians, we must continue our interest in general medicine and the specialties although the actual practice may be restricted to a single specialty.

Mr. John Henry, in room 410 has been admitted because a large prostate has made micturition impossible, but he expects me to keep in mind that his other annoyances also require attention. One of his other troubles is chronic bronchitis which often interferes with his sleep. The answer to the title question is perfectly clear.

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Scientific Papers

THE DISEASE OF DIABETES

PANEL DISCUSSION*

MODERATOR: J. Sheldon Eastland, M.D.
PANEL MEMBERS: Garfield G. Duncan, M.D.
Joseph T. Beardwood, M.D.
E. Paul Knotts, M.D., *presiding*

Dr. E. Paul Knotts: This part of the program will be a Diabetes Panel. Dr. J. Sheldon Eastland, Associate Professor of Medicine, University of Maryland School of Medicine, will act as Moderator. I shall ask Dr. Eastland to present his associates and participants in this panel.

Dr. J. Sheldon Eastland: I have the great pleasure in introducing our speakers today, both of Philadelphia. Dr. Garfield G. Duncan, Clinical Professor of Medicine, Jefferson Medical College, Director of Medical Division of the Pennsylvania Hospital and the Benjamin Franklin Clinic in Philadelphia. To my right, far side, Dr. Joseph T. Beardwood, Professor of Metabolic Diseases, Graduate School of Medicine of the University of Pennsylvania, Director of Medical Services, Abington Memorial Hospital, Abington, Pennsylvania.

We arranged to have a small Panel in number so that we could have the addresses first and then throw the meeting open to questions. Diabetes is such a general subject that probably many will have questions they'd like to have discussed. Our speakers have very kindly agreed to discuss any phase of diabetes, not confining it entirely to what is listed on the program. Therefore, I hope you all will take the opportunity to ask these men, well learned in diabetes, questions.

This disease of Diabetes we are to discuss this afternoon, of course is not a rare disease at all. Everyone has seen cases and many of them. It is estimated there are probably at least a million people in the United States who have and know they have, diabetes. From spot surveys we estimate there is another million people who have diabetes and are unaware of it. Therefore, our duty as physicians is then two-fold.

First, we want to treat these people who we know have diabetes, and secondly, we want to detect the unknown and therefore untreated, group with diabetes. Considerable progress has been made in recent years in finding this group of unknown diabetics.

One way, of course, has been by educational campaign. Informing the layman of the signs and symptoms of diabetes and when they are found have him consult his physician.

Another method which has been I believe, rather productive, has been the detection drives. Here, as you all know, our Faculty has a Committee on Diabetes which has conducted detection drives for several years during Diabetes Detection Week which is sponsored largely by the American Diabetic Association. Our results have been very encouraging.

Today our chief interest is the treatment of the known diabetic. This group of people is

* Presented at the One Hundred and Fifty-sixth Annual Meeting of the Medical and Chirurgical Faculty of the State of Maryland, on Wednesday afternoon, April 28, 1954, in Osler Hall, 1211 Cathedral Street, Baltimore 1, Maryland.

largely in middle age; as we know, the incidence of diabetes is high after the age of 45 years. These elderly or middle age people occupy a very important position in life in our labor force. The Metropolitan Life Insurance Company has gathered some statistics and they estimate there are probably about 250,000 people employed in the labor force today with diabetes, and the number increases every year.

These people, as I said before, are an important group. They have become established in life and they play an important role in industry. Therefore, we should do everything we can to see that they get proper treatment.

The diabetic carries out the major portion of the treatment himself. He directs and follows his diet, he examines his urine specimen, and he gives his own insulin if it be necessary. The physician more or less acts as a guide or consultant, and for that reason the treatment of diabetes should be made as simple as possible and we will have better cooperation.

The basic factor in the treatment of diabetes is the diet. Probably forty or fifty per cent of the people with diabetes can be controlled with diet alone. In the past years there have been innumerable types of diets used here in Baltimore. I think if you would go from one hospital to another you would find each hospital passing out to the patient leaving the hospital, a form of diet different from that of another.

When these people return home and begin to compare their diets it becomes most confusing. In my opinion that one thing has been the basis for poor cooperation; not understanding the diet. In many instances I have wondered if the doctor understood the diet.

Recently a nation-wide effort has been made to clear up this subject of diets. A committee of representatives from the American Diabetes Association, the American Dietetic Association, and the Diabetes Section of the U. S. Public Health Service, got together to work out this problem. After several years they came forth with what I believe is some very valuable help. What they accomplished is noteworthy and I'm going to read their conclusions.

1. A short table of food values for calculating the composition of diabetic diets.

2. A set of six exchange lists which contain foods of similar composition and which therefore may be substituted for one another, making the diet workable to the patient.

3. Easy method for calculating diabetic diets based on these food and exchange lists.

4. Six sample diets at different caloric levels with varying amounts of carbohydrates, protein and fat. These diets are most workable. I believe the physician who knows very little about handling diets can work with these without the assistance of a dietitian and accomplish a great deal.

5. An illustrated diet book which is entitled, "Meal Planning with Exchange List," for the physician to give to his patients so they can manipulate their diet. These diets have been named the ADA Diets. Sometimes we hear them called Exchange Diets but I think ADA is probably the most universal term.

Fortunately the acceptance of these diets has been very great and the results most gratifying. As I mentioned before, however, diet alone will not bring about satisfactory control of all diabetes. Probably forty to fifty per cent can be controlled with diet but the remaining group needs something else and that something is that life-saving material known as insulin. Today we are very fortunate in having Dr. Garfield G. Duncan with us who is going to discuss insulin therapy.

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INSULIN THERAPY FOR DIABETES

GARFIELD G. DUNCAN, M.D.

Dr. Eastland, Mr. Chairman, Ladies and Gentlemen, in these opening remarks I wish to make it clear which diabetic patients I believe should be given insulin and those which should not. I have followed a rough plan of dividing the patients into those having mild and those having more severe diabetes.

The patient has mild diabetes if he is overweight and has never received insulin. Of course if he had been thin and had become overweight by virtue of treatment with insulin, that wouldn't make the diabetes mild. But, in general, it is safe in saying that the untreated, overweight diabetic patient has a mild diabetes and barring acute complications will not need insulin.

Now, how important is this group? About eighty per cent of diabetic patients when they consult their physician for treatment first are overweight, and while Dr. Eastland said that probably fifty per cent of the diabetic population could have the diabetes well treated by diet alone, we could raise that percentage if full cognizance is taken of the advantage of proper treatment when the patient first comes for treatment, because eighty per cent are then overweight. Insulin can be avoided in these cases by utilizing a reducing program. Those of the profession who do not like reducing programs call them starvation programs. I don't care what one calls them, the fact of the matter is if an individual is obese he should reduce and the best way to reduce a diabetic patient is to restrict his caloric intake. If you don't restrict his caloric intake, sooner or later he will start to lose weight on his own, because of the activity of the diabetes.

Nearly every thin adult diabetic that you have occasion to see, will give you a history of having been overweight at one time. At that time he had a trump card to play. He could have pushed his diabetes off the platform by reducing his weight through reduced caloric intake, but he didn't do it and he wasn't advised to do it, and as a result he went along and then suddenly began to lose the weight rather quickly and at first, he or she was quite pleased, but as the weight reduction continued became alarmed and started treatment when their weight was below normal. The diabetes is then severe and they lost the opportunity that could have been gained through a reduction in weight by virtue of a reduced caloric intake. The fat diabetic is a mild diabetic and, barring acute complications, the diabetes can be controlled successfully by reducing his caloric intake without insulin.

The diabetes may be so well controlled by a reduction regime a normal response to a glucose tolerance curve, may be obtained as was shown by Dr. Newburgh and his group two decades ago. One shouldn't be misled into thinking that the patient is cured of his diabetes. He isn't, because if his weight comes back the diabetes puts in its appearance again.

Now, the thin patient and the child diabetic, they can't afford to lose weight. They will not do well on a low calorie diet. In fact, to provoke normal growth on the part of the child, and normal health on the part of the thin adult, you want them to increase their weight; to achieve this, insulin is necessary and so, all child diabetics require insulin because they are going to grow, their body mass is going to be greater; their total metabolism is going to be greater, they will need more insulin, and the same, in general, is true of the undernourished adult diabetic. So then, of those without complications the thin diabetic and the child diabetic must take insulin.

Most papers pertaining to diabetes deal with the subject of Insulin Therapy. I'd like to emphasize that not enough attention is given to the eighty per cent whose diabetes could be

controlled without insulin when they first seek treatment. You might say, is there any harm in giving these overweight patients insulin? Dr. Joslin gives insulin to overweight patients and he knows an awful lot about diabetes. I have great respect for him, but I don't like to give the overweight diabetic, barring acute complications, insulin, for several reasons. The first is, it is very difficult to get them to adhere to a reducing program while they are taking insulin and so their weight will not decrease in most instances and that is bad. It is bad for the nondiabetic and it is worse for the diabetic. Treatment with insulin tends to prevent a wise reduction in weight.

Secondly, most of these overweight patients to whom you give insulin never give it up. I have seen patients that have taken insulin seventeen, eighteen and twenty years who got along very well without it when they reduced their weight by ten to twenty pounds. Also, it is very wasteful to give insulin to obese patients who would do better without it.

If you take a thin diabetic with a blood sugar of 250,—the thin diabetic, according to my classification has a more severe diabetes because he must have insulin, than the fat patient—and a fat patient with the same level of blood sugar and give each of these patients the same amount of insulin, a much greater reduction in the level of the blood sugar occurs in the thin patient than in the fat patient. This is because fat patients tend to be very resistant to insulin. It may take 80, 100, or 150 units to control the diabetes in a fat patient with mild diabetes when actually if his weight is reduced he will not need insulin.

Once a patient has taken 80 or 100 units of insulin, one is very apt to think, my patient has severe diabetes because he takes so much insulin. That, of course, isn't so. From the fat diabetic without acute complication, you can withdraw 100 units of insulin abruptly and very little happens. He may lose four or five grams more sugar in the urine for a few days, but if you put him on a low calorie diet, even that will clear up.

Now, you dare not do that with a child diabetic or most thin diabetics. They will be in trouble in a few days. Towards the end of World War II, many of you may know that there was considerable alarm about the decreasing supply of insulin. Actually, I'm told that there were only two weeks supply of insulin in this country when the restrictions were lifted on the meat production. Of course they could have replenished that supply quickly if all would stop giving insulin to their fat patients and reduce them instead, and at the same time prolong their longevity, according to the indications in Life Insurance statistics.

We have then, the child diabetic and the thin diabetic to whom we are going to give insulin from the outset of therapy. Now, which insulin? I am not going to complicate the insulin therapy. I'm merely going to outline what I have found the simplest and most effective means in controlling the diabetes with insulin and it boils down—I'm still talking about uncomplicated diabetes—it boils down to three different programs.

A fairly small percentage of these patients needing insulin do very well with one dose of an intermediate acting insulin that is globin insulin or NPH insulin or Lente insulin—given three-quarters of an hour or an hour before breakfast.

The percentage of patients who have good control throughout the twenty-four hours with that single dose is small, but there is a sufficient number of them to make it worth mentioning.

The second plan, and the plan that we use for the diabetes with a little greater grade of severity, is a mixture of NPH insulin and regular (unmodified or soluble or crystalline) insulin given a few minutes before breakfast each morning. A considerably larger group of patients is controlled with this program because regular insulin, in the first place, works rapidly and prevents the hyperglycemic phase in the fore-

noon which is likely to occur in this group unless a rapidly acting insulin is given.

The third program, and the one we use for the most severe diabetes, is a mixture of NPH insulin and regular insulin, before breakfast with a small dose of NPH insulin after supper.

Now, when you have that combination and if you are having the urine tested before each meal and at bedtime, it is easy to know what to do with the insulin. If sugar appears before lunch regularly, it is the regular insulin in that mixture in the morning that should be increased. If sugar appears before supper, it is the NPH insulin in that mixture that should be increased. And if sugar appears in the first specimen voided in the morning, it is the small dose of NPH insulin given after supper that should be increased. Each section of the day is well-covered with that program.

Best results are obtained if the diet is divided in a uniform manner. Formerly we used several ways of dividing the diets. Now we divide the diets the same for every patient no matter what insulin program he is on. We ask the dietitian to divide the prescribed diet into three equal meals, breakfast, lunch and supper, and take a bread and milk exchange from breakfast, to be taken around four p.m., and a bread and milk exchange from the supper to be taken at bedtime. That reduces the size of the breakfast and decreases the likelihood of hyperglycemia before noon. Nourishment at 4 p.m., reduces the likelihood of a hypoglycemia before supper and permits a bigger dose of intermediate-acting insulin before breakfast than you could give if you did not give nourishment at 4 p.m., and the nourishment at bedtime will reduce the likelihood of hypoglycemic reactions during the night.

This is really a combination of a good old American and a good old British custom of having afternoon tea on the part of the British and the bedtime snack on the part of the Americans. I think it is important that use should be made of this distribution of the diet because it permits you to get smooth control of the diabetes when you could not do it as well without it.

The excuse is often given for lax treatment on the grounds that they don't want to get the diabetes too closely controlled. So the patient is allowed to eat pretty much as he wants to, and enough insulin is given to keep him from getting into acute trouble. That is a poor excuse. I am quite sure that advantage should be taken of the proper distribution of the diet and the proper combinations and distributions of the insulin if your patients are going to get the best results.

I think there were one or two at least in the audience who thought I was going to mention a free diet, and I shouldn't disappoint you because it reflects one's feelings whether or not he thinks diabetes should be controlled. I think the diabetes should be wisely controlled with diet alone when practicable and with insulin added when necessary.

The big handicap, for those who use free diets, allowing the patient to eat what he wants to and giving them only sufficient insulin to prevent them going into ketosis, is that they have no controls because none of the severe diabetics have a controlled diabetes.

Those of us who believe that the diabetes should be controlled, have a large group of patients, who do as they are told. In these, diabetes is well controlled. But, we have also a much smaller group who go on the free diet on their own, and so we have these two groups ahead of us all the time, our own group where they do as they are told, and the other group on the free diet, and it is from this small group on the free diet who do as they like, that account for over seventy per cent of my readmissions to the hospital.

The three plans of insulin therapy mentioned are quite satisfactory but may be over-simplified. For that group of patients having severe diabetes and to whom we are giving NPH and regular insulin before breakfast and a dose of NPH insulin after supper, the patient, or you, may wish to eliminate that evening dose. When

the diabetes is controlled on this program, what one may do is to add up the total number of units and try a two-to-one mixture—two of regular insulin to one of protamine zinc insulin. That, to my way of thinking is the only place protamine zinc insulin has in the treatment of diabetes now. That is when it is used as a mixture. Because if the diabetes happens to be controlled satisfactorily with a single dose of protamine zinc insulin before breakfast, I maintain that the patient would be in greater safety if a single dose of an intermediate acting insulin were given instead, because it works most effectively during the day when three meals come in close succession, whereas protamine zinc insulin is more likely to expose the patient to hypoglycemic reactions between midnight and breakfast time. We have long since abandoned the use of the protamine zinc insulin as a single type of insulin.

With the two-to-one mixture, in about ten to fifteen per cent of cases, you get satisfactory results. Hence there is a very definite place then for a two-to-one mixture, two of regular insulin and one of the protamine zinc insulin when it is effective. If it isn't effective you can merely revert to the program that you know was a little less simple, but one with which you had a little better control and was effective.

I recall a medical student having a great deal of difficulty controlling his diabetes. He had been taking four injections of insulin daily. We controlled his diabetes with 150 units, a combination of NPH and regular in the morning, and NPH after supper. Then changed to 100 units of regular insulin and 50 units of protamine zinc insulin. That was several years ago, and so far as I know he is still taking the same program and his diabetes, the last I heard, was under excellent control.

There are other combinations, too, that one may find individual patients responding to very well. A rice farmer from Crowley, Louisiana, taught me one combination. I just mention it, not with the idea of complicating the treatment but merely to emphasize that there are other ways of doing it. This man was taking a mixture of NPH and regular insulin before breakfast and a small dose of NPH insulin after supper. He fought against this evening dose, and maintained as how protamine zinc insulin being apparently most effective during the night, why couldn't he take a dose of protamine zinc insulin in addition to the NPH and regular insulin before breakfast. It still meant two injections. I had no objection to his trying it and he has been on that program now for two years, and I have about a dozen patients who are taking NPH and regular insulin and a small separate dose of protamine zinc insulin before breakfast.

Now, if we move to the complications of diabetes and the part that insulin plays in it, let us assume that you have your patient on one or the other of these programs of insulin therapy, and he develops an acute sinusitis or some other infection of mild degree. It may well be that all you need to do is increase the insulin in each of the doses that he is getting, so that merely stepping up the regular insulin and the NPH insulin in the morning, and by increasing the NPH insulin after supper may suffice for the milder infections.

A second plan, if the patient is a little more acutely ill, is to maintain his old program exactly as it was and give him a small dose of regular insulin every four hours until the glycosuria is corrected and then gradually decrease and stop it. That is a simple way of controlling moderately severe infections at home.

For patients who are admitted to the hospital with acute complications which are usually more severe, we don't use either of those programs. We prescribe the diet that we would like the patient to have and have the dietitian divide it into four equal feedings, one feeding every six hours. Six a.m., twelve noon, six p.m., and twelve midnight, and we give regular insulin before each of those feedings. If he comes in, let us say, at ten o'clock in the morning, and he has already taken his usual dose of combined NPH

and regular insulin in the morning, but because of his acute infection he has a marked degree of hyperglycemia and glycosuria, we would give one-third of his total dose in the form of regular insulin before the midday meal, and we would collect the urine specimen from twelve noon until about five-thirty in the evening and the amount of sugar in it would decide whether we would increase the insulin before supper or not. If he still had four plus sugar in the urine at that time, we might add ten or even twenty units if the dose were big. The diabetic status is reëvaluated in this manner at six-hour intervals as far as the insulin is concerned, and the increases should be made rapidly if necessary.

When the infection subsides and the fever subsides, you can revert abruptly to his former program and, with minor adjustments, the diabetes will be controlled.

There seems to be considerable fear on the part of residents in making a change abruptly at that time. As a matter of fact the patient is in no danger at all from the diabetes getting out of control for a day or so, providing the acute infection has completely subsided.

In conclusion I would like to emphasize the need to make the obese diabetic reduce his or her weight. If you give insulin to such a patient, make him stick on a reducing program; you'll find it almost impossible because the patient is going to give the credit to the insulin he is getting and not to the reduction regime. As a result he is likely to maintain a weight which will reduce his longevity. Then there is the classification of the diabetics—the obese with mild diabetes and the child or thin diabetic who must have insulin; and the three different programs of insulin therapy that will control all grades of severity of diabetes in the uncomplicated state.

Now, if you do all of this according to the plan that I have outlined, there won't be any need to treat the patient for ketosis. But, assuming that some of you are going to fall short of that, I think it is well to ask Dr. Beardwood to go ahead and give his talk in the management of ketosis!

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DIABETIC ACIDOSIS

JOSEPH T. BEARDWOOD, JR., M.D.*

The four most frequent causes of mortality in the diabetic have been (1) infection, and/or gangrene, (2) acidosis, (3) tuberculosis and (4) disease of the cardio-vascular and renal systems.

Infections are now relatively easy to control since the advent of the antibiotics. Tuberculosis, with the antibiotics and other newer chemical means of treatment, now seldom presents a threat to the life of the diabetic.

Acidosis, which was formerly the greatest cause of death among diabetics and very often precipitated by infection or tuberculosis, should not, but frequently does, remain a problem in the care of the diabetic. The atherosclerotic cardio-vascular complications of diabetics have now assumed a most important role in the mortality and morbidity in these patients. This is a late complication and in certain types of cardio-vascular renal disease, such as diabetic nephrosis, is probably peculiar to the diabetic. However, we feel that adequate control of the diabetes over the years plays a very important role in the prevention or postponing of the atherosclerotic picture.

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In reporting a series of diabetic acidosis in 1941 (1), (JAMA, Nov. 15, 1941, Vol. 117, pp. 1701–1704), we stated: "Since the introduction of insulin, physicians have been apt to feel that diabetic acidosis is a rare and unusual complication of diabetes and that it no longer presents a frequent medical problem. Unfortunately, this is not true. It is still of major importance, and as a careful study of the literature will reveal, is still responsible for a large number of fatalities which in most cases could be avoided if physicians and the laity were conscious of the incidence and the early symptoms." This statement still holds true, but I am glad to say, to a lesser degree. Whereas in 1941 we reported 220 cases of diabetic acidosis occurring in 1865 diabetic hospital admissions, or about 11%, during the last four years, on the Metabolic Services of the Graduate Hospital of the University of Pennsylvania, Philadelphia, Pa., the Abington Memorial Hospital, Abington, Pa., there were admitted 2098 diabetic patients, of whom 107 were admitted in acidosis or approximately 5%. This represents just about half the number of acidotic admissions seen before 1941, which I feel is due to two definite factors:

1. The early use of antibiotics in infections which frequently lead to acidosis, and
2. A more alert profession, intelligently educating their patients, to take care of their disease and be alert for complications.

Etiological Factors

In our experience the most frequent etiological factors in the production of acidosis have been (1) infection; (2) irregularity with the routine, particularly the omission of insulin. We have not been impressed that patients who are taking insulin, especially those on fairly large doses, will develop acidosis by disregard of their diet alone. (3) A group of other conditions, such as endocrine imbalance, i.e., onset of menstruation, pregnancy, development of hyperthyroidism, and (4) a surprisingly large number of patients develop acidosis without knowing that they have diabetes and this is particularly true in the younger age groups. Acidosis often develops as a late complication in diabetic nephrosis and at times may be a terminal state in this condition. This terminal acidosis, however, is complicated in most cases by impending uremia and while the acidosis may be corrected, the uremia will oftimes prove to be the cause of death. Patients with Kimmelstiel-Wilson's disease usually will die of a terminal uremia or a vascular accident. So frequently is acidosis caused by infection that in a case of acidosis developing without any demonstrable cause, "hidden" infection should be sought.

Symptoms

The symptoms of diabetic acidosis are important to remember. Diabetic acidosis does not develop rapidly, but usually requires 24 to 48 hours before coma results during which time the symptoms are:

1. Increase in the cardinal diabetic symptoms are polyuria and polydypsia.
2. The abdominal symptoms; nausea, vomiting and abdominal pain. This may be associated with localized areas of tenderness in the abdomen and at times pain in the thighs. As this is also associated with leucocytosis and at times fever, it is quite understandable why many cases are thought to be cases of acute abdominal emergency.
3. Drowsy restlessness.
4. Development of Kussmaul breathing.
5. Increasing stupor.
6. Unconsciousness.

These symptoms may not necessarily occur in this order, but we have been impressed that at least 75% of the patients we have seen have had abdominal symptoms at a relatively early stage.

Diagnosis

The diagnosis of diabetic acidosis is an easy one to make with laboratory aids, and is made earlier if one is conscious of the fact that it may

occur in any diabetic and that it may be the cause of the above symptoms in a patient who does not know that he has diabetes. We depend more on the blood chemistry for our diagnosis and also for following the treatment. The presence of acetonuria alone is not sufficient evidence that ketosis exists. However, the presence of both acetone and diacetic acid in the urine is a very suggestive finding.

It is important to consider that diabetics become unconscious for other reasons than acidosis, such as cerebrovascular accidents, concussion, hypoglycemia and all the reasons causing unconsciousness in non-diabetics. One should be sure of one's diagnosis before starting to treat the cause as acidosis, although some of the causes of unconsciousness, such as cerebrovascular accidents, may precipitate acidosis.

A careful history of the onset of unconsciousness is of great value, remembering that any sudden development of coma without premonitory symptoms is seldom due to diabetic acidosis. A patient who is in diabetic acidosis will usually have Kussmaul breathing, dry skin, beefy red tongue, soft eyeballs and usually a rapid and at times irregular pulse. If it is impossible to obtain urine or blood chemistry at the time the patient is seen, doing a white blood count ofttimes will be of value. This is elevated in diabetic acidosis anywhere from 10,000 to 30,000 and is seldom elevated in other conditions, which must be considered in the differential diagnosis. If there is any doubt as to whether the patient is in hypoglycemia or diabetic acidosis, by far the safest procedure is to give the patient glucose, which, if the coma is due to hypoglycemia, will usually produce a dramatic improvement, and if the patient is in diabetic acidosis will not do any great harm.

Treatment

The best treatment of diabetic acidosis is its prevention, and the best method of preventing acidosis is to properly educate patients to appreciate its early symptoms. Also it is important to remember that any diabetic is a potential case of acidosis, and if they are alert to the early symptoms and seek aid promptly, many cases can be aborted. One of the most severe cases of acidosis that we have seen associated with pregnancy occurred in a nurse who was a juvenile diabetic and for some years did my diabetic instruction work. She married and discontinued work. In about one year she had become pregnant, went into severe acidosis and was admitted with a CO_2 of 2 mEq., and fortunately responded to treatment. On recovery she was chagrined and surprised and her comment was typical, "I didn't think it could happen to me." Obviously there is a happy medium between the patient who lives all his life in fear of the development of acidosis and those who after several months of normal diabetic life forget all about this possibility.

Diabetic acidosis, particularly if it is of long standing or a very severe degree, represents a marked disturbance of fluid and electrolyte balance. It is a condition in which this marked disturbance occurs before treatment and ofttimes further electrolyte imbalance is produced by the active treatment of diabetic acidosis. It is much more than a condition of insulin deficiency and salt and water depletion. A consciousness of the changes that may take place, and adequate chemical appraisal at frequent intervals, are essential parts of the proper diabetic care.

The treatment of diabetic acidosis is a somewhat individualized procedure. As a rule, in the average case, however, the following is our routine:

1. A blood sugar, CO_2, blood urea nitrogen and chlorides are done immediately on admission.
2. *Insulin.* Insulin dosage will vary depending upon the patient's age, previous insulin dosage and also whether or not the patient is an unknown diabetic. Usually, however, if the blood sugar reading is 250 mgs. or higher, 100 units of insulin is given every half hour for three doses.

3. *Lactate.* We immediately start at 0.6 m. sodium lactate. If the patient is an adult we initially give 1000 ccs. and if a child, 500 ccs.
4. *Laboratory Follow-up.* We repeat the blood sugar and CO_2 determination in two hours, at which time we are more concerned with the acidosis than the glycemia. If the plasma CO_2 has failed to rise more than 8 volumes % or 3.5 mEq., we administer one-half the original amount of lactate. Insulin is again administered in amounts from 50 to 100 units every hour, depending upon this blood sugar determination.

   Blood sugar and CO_2 determinations are done again after two hours, and the treatment from here on varies a great deal, dependent upon these laboratory findings.

Unless the patient has responded clinically and is taking oral feedings, we also do a blood potassium in three to five hours after admission. There has been a great interest recently in hypopotassemia in diabetic acidosis. In 1933, Astley first called attention to this possibility. This is seldom seen before four to six hours of active treatment. It occurs because of the increased glycogenolysis and gluconeogenesis, which results in a shift of potassium from the intracellular space with the profound diuresis which results with treatment, many of these intracellular ions are washed out. Crampton et al. (2) (Diabetes, ADA Journal, Vol. 2, No. 1, January–February, 1953, pp. 1 to 7), have pointed out that during therapy there occurs: (1) rehydration with expansion of the extracellular space and dilution of the potassium; (2) re-establishment of urinary excretion with further loss of potassium and (3) a movement of potassium into the cells during glycogen storage and cellular rehydration.

These investigators feel that hypopotassemia is such a serious complication that methods for its prevention should be undertaken, and they give potassium in the form of dibasic potassium phosphate, prophylactically, to all acidotic admissions to replace the phosphorus as well as the potassium loss. The occurrence of this condition has been adequately proven to exist by many investigators. The clinical symptoms of this condition are varying degrees of skeletal mass muscle paralysis of the flaccid type with or without respiratory distress, vascular collapse, and an increasing persistence of nausea and vomiting.

We have not used potassium prophylactically, but do a blood potassium at the end of four or five hours and, if indicated, administer potassium chloride as 1% solution intravenously if there is adequate kidney output, as we believe that if patients can be gotten on oral feedings early, hypopotassemia is not likely to occur.

Serial electrocardiograms will also be of value in determining hypopotassemia, but there is considerable question as to whether they are accurate or pathopneumonic. A prolongation of the QT interval and a flattening of the T-waves are very suggestive of this condition. To properly evaluate these tracings, however, an electrocardiogram should be done on admission and compared with those done at three-hour intervals.

5. Blood sugar and CO_2 determinations are carried out every three hours until the patient is at a safe level and insulin and fluids are administered as indicated.
6. There are other adjuncts which are used in certain cases. If the patient is markedly dehydrated, hydration is accomplished with normal saline solution subcutaneously or intravenously, and after several hours we may in certain cases give 10% glucose in saline or water intravenously, if the patient is unable to take carbohydrates by mouth, to stimulate urine filtration.

In our experience, the use of alkali, i.e., sodium lactate and in certain cases sodium bicarbonate, has not been attendant with any danger and indeed, we feel it is correct thinking to promptly restore the chemical balance and correct the cerebral anoxemia. In any series of cases, in which the use of alkalies are compared with the hydration by saline alone, the time required to

correct the acidosis is much less in the alkali treated cases. Continued cerebral anoxemia may result in permanent brain damage, so that we feel the sooner this is corrected the less permanent damage remains after an attack of severe acidosis. We also feel that the quicker chemical response obtained with alkalis resulting from the prompter feedings by mouth decreases the tendency to the development of hypopotassemia. It has seemed to us that with the use of such a program as outlined above, we have seen less clinical or chemical evidence of potassium depletion than has been reported by investigators not using alkalis. We have seen no contra-indication to the use of glucose and indeed, if one is careful checking the chemistries, it is difficult to imagine any untoward effect from its use. High blood sugar per se has never been the cause of fatality.

7. If the patient is in "extreme" acidosis, i.e., with a shock picture, unconsciousness, low blood pressure, leaky skin, we will start oxygen and plasma. It is important to consider that the degree of unconsciousness does not altogether parallel the plasma CO_2 combining power, but depends upon the lack of oxygen exchange in the brain tissues. In patients with this clinical picture, a sodium chloride determination is of great value as many have extreme degrees of hypochloremia, and hypertonic saline is often of great help.

Other adjuncts of treatment are:

Gastric lavage, if vomiting continues; further use of saline solutions if dehydration is extreme. Many patients in acidosis have various types of cardiac irregularity which are seldom helped by the use of digitalis, but which usually restore themselves to normal with the correction of the chemical imbalance. While the shock picture in acidosis is not unlike that seen in the crisis in Addison's disease, our experience with the use of cortical extract or other similar preparations has been discouraging.

Mortality

In the 107 cases reported here, there were two deaths, one of which occurred three hours after admission to the hospital in a patient, who for some years had taken about 50 units of insulin a day and had stopped his insulin three days before admission. The other was in a woman of 52 years, who had had a severe coronary thrombosis and at the time of her death had a CO_2 of 12 mEq. I think this mortality record reflects very definitely the ability to control infection in the presence of acidosis and possibly to add continuing awareness of the value of obtaining the full chemical picture in these cases.

Conclusions

Diabetic acidosis is a diminishing, but ever present threat in the diabetic. With the aid of antibiotics, mortality rate is greatly improved and by proper education of the profession and laity, the incidence of its occurrence can be greatly diminished.

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CLOSING REMARKS

Dr. Eastland: This is our State meeting, and we have men here from all parts of it.

From what we gather in Philadelphia, it seems that the suburban and rural man is having more acidotic cases than the doctors in the city; I wonder why? I presume in the city many patients are coming to clinics and the clinics are attempting a greater educational program.

I believe that one of the basic things in the treatment of diabetes is education of the patient

to take care of himself. We wouldn't have acidosis, or else very little, if the patients coming into our hospitals had received the fundamental principles of diabetic management.

Today, there are a lot of simple primers or textbooks that could be put into the hands of the patients and I think they would read them. My experience with diabetics is that they are very anxious to find out about their condition, and all you have to do is put something in their hands. I realize that the man who is in general practice cannot take a lot of time to sit down and explain all the phases of diabetes to every patient, but I do think if he would put into their hands some of these simple primers, that the results would be very rewarding.

The testing of urine has been simplified. Today we do not have to bother with the old test tube, trying to boil it over an alcohol lamp and having the contents jump all over the room. We have simple tests but the patient must be instructed as to when to collect and test specimens. I have noticed quite frequently, even right in the hospital, for example, the point Dr. Duncan mentioned—the specimen collected before meals. That can be the most misleading specimen, I think, if you do not say a little bit more. The individual had his breakfast, voiding before breakfast, and he does not void again until just before lunch. When we test this specimen it contains sugar, and particularly that patient taking NPH insulin. The sugar was spilled probably about the first hour or two after his breakfast, but just before lunch he had become sugar free. If we test that specimen and find it positive for sugar, are we safe in increasing the morning dose of NPH insulin? Maybe we need something else! Maybe if it be true that it is positive, increase of the NPH would be the thing to do, but if it is negative just before his lunch, probably as Dr. Duncan said, too, it would be better to add some regular insulin. I have had trouble in hospitals getting my specimen collected well. I think the same thing applies in the home. Instruct the patient when to collect the specimens that will be of the most value. Better cooperation will be obtained if the diabetic is not given too many specimens to test.

I find that many diabetics get into trouble with their feet. They have callouses, corns, whatever you want to call them, and do they know how to handle them. It seems very simple and we all know all about them but the average layman knows nothing about them. He still buys corn plasters and gets into all kinds of trouble with infections on his toes. I think we should teach him care of his feet and we would avoid gangrene to a big degree.

Today, with our diabetics living so much longer, we are getting vascular complications; namely, eye changes, coronary changes, changes in the vessels of the lower extremities and kidney changes. The changes in the vessels of the lower extremities are the ones that lead to gangrene, and therefore we want particular attention paid to the feet.

We couldn't, of course, cover the whole subject of diabetes, but I think Dr. Duncan and Dr. Beardwood have reviewed the field very thoroughly.

I believe paper has been passed out. If there are any questions that you might want the panel to discuss please write them out.

DISCUSSION

DR. KNOTTS: May I suggest the possibility that the higher incidence of poor control, as evidenced by acidosis in the rural group as opposed to the urban group, might at least in part explain the fact that—certainly I can speak for the Eastern Shore—the people are more reluctant to give up their gracious way of life. They are more difficult to regiment and even the doctor is likely to assume an attitude of *laissez-faire*, in his conduct of the case. I have a question which I would

like to ask relative to relationship of diabetes to lipid diseases, cholesterol in particular, the incidence of juvenile arteriosclerosis and the relationship of diabetes to lipid disorders. You may answer that or refer it to the colleagues, as you wish.

DR. EASTLAND: Dr. Beardwood, you have spoken on acidosis and probably should answer this question.

DR. BEARDWOOD: The relationship of blood lipids in diabetes and the role lipids play in atherosclerosis in diabetes is an interesting, but unanswered question. It is a common finding in a new or controlled diabetic to have a hypocholesteremia and disturbance in the lipids and with this, particularly in juvenile diabetics, have hepatomegaly which is probably due to a "fatty" liver.

It has been our experience that as the diabetes is controlled without any great attempt made other than our normal diet program which contains probably eighty to ninety grams of fat, that there is a diminution in the blood cholesterol and in many of these children and adults, diminution in the size of the liver. There are a few patients, however, in which hypercholesterolemia and marked disturbance of the fat metabolism occurs in the diabetic, this case which I showed you the history of was one such case. She continued to run a high blood fat and continued to require large amounts of insulin. This is a rare complication. There has been some very interesting work reported by Dr. Hurst, in which he has shown that the lipids and phospholipids which are the fraction more at fault in atherosclerosis, vary with the level of blood sugar and control of the diabetes in experimental animals and man. This, Dr. Duncan and I, like very much because it proves what he and I believe, that control of the diabetes is a very important factor in prevention or postponing the development of arteriosclerotic complications.

I would say that the average diabetic who is first seen with an elevated cholesterol will show a return to normal valves as the diabetes is brought under control with the proper diet and insulin. Certainly we don't know too much about some of the atherosclerotic changes, but in view of this work which has been recently done, it would seem that the phospholipids are an important factor, but that most of the elevated lipids tend to return to normal with the control of the diabetes. Does that answer your questions?

DR. KNOTTS: I am sure that every person and every doctor here does treat diabetes and this is your opportunity to clear some perplexities that you may experience. We have here a Panel which I am sure can answer the questions and we wish to invite them.

DR. EASTLAND: We have some questions here.

Q. Is it true that one detects early diabetes more readily by taking blood sugar determinations 1½ to 2 hours after breakfast rather than fasting blood sugars?

ANSWER: I think that it is pretty true that by that means you will catch some cases that you will miss entirely on fasting blood sugars. On the screening programs we try to encourage the patient to come to the center at least an hour-and-a-half or two hours after a meal. The fasting blood sugar has been the old method and hard to get away from, but I believe without any question—I don't know how the other members of the Panel feel but the 1½ to 2 hours specimen would be better. Are you all agreed on that?

DR. DUNCAN: I'd like to add just a point on that. I agree thoroughly with the remarks that were made, but there is quite a number of individuals who belong to diabetic families or they may have had sugar in the urine at one time in the past, and the test that has been mentioned either fasting blood sugar or blood sugar taken 1½ after meals may be normal. You get much better proof that that patient has not diabetes or has diabetes, I think, if one uses a modified glucose tolerance test. We have been using this now for six years and like it very much. We give 100 grams of glucose, the same for an ordinary three hour glucose tolerance test and we take one blood sugar, two hours after the 100 grams

are given. If that blood sugar is normal then we can reasonably say that that patient has no detectable evidence of diabetes. My reason for mentioning this test is that it is a simple program which requires only one blood sugar determination. It will probably be used much more frequently than if one is obliged to do five tests as is the case with the orthodox three-hour glucose tolerance test.

Q. DR. EASTLAND: What is the simplified routine for treating diabetic acidosis by means of serum acetone?

DR. DUNCAN: Of course I have paid a great deal of attention to the serum ketones. They are easily determined. You can make a correct diagnosis of diabetic coma in a farmhouse if you want to. All you need do is to find 4-plus glycosuria; this done, draw off 10 cc. of blood in an oxalated tube and let it stand five or ten minutes, get one drop of clear plasma on the top, and test it for ketones. If the test reveals a 4-plus reaction, that patient is in diabetic coma. Nothing else will give those two findings 4-plus glycosuria and 4-plus plasma ketones. Then you can safely give the patient 100 units of regular insulin at once and eight ounce of salty broth and transfer him to a hospital.

I remember one patient for whom the onset of treatment was delayed eighteen hours to confirm the suspicion that she was in diabetic coma. Fortunately she survived.

As for treatment, when the patient gets into the hospital, and we find a 4-plus reaction for plasma ketones, then we dilute that plasma, one-to-one with water or saline, and if that dilution gives 4-plus reaction for plasma ketones, then that is a more severe ketosis. Then we dilute the plasma still further again one-to-one and if this second dilution gives a 4-plus reaction for ketones, then the patient is in profound coma, and under those circumstances we give 300 units of regular insulin at once. Tests for plasma ketones give us a means of early diagnosis, and are a guide to the initial dose of insulin. And then if you test for plasma ketones from hour-to-hour, the first improvement that you will detect will be a decrease in the ketones in the diluted specimens of plasma and when the undiluted plasma gives less than 4-plus reaction for ketones, the resistance to insulin has disappeared. It is imperative to reduce the insulin abruptly and spread the doses. We have this third feature then, plasma ketones are a guide as to when to let up on the insulin administration, and we consider that to be very important. This test is a more reliable guide than the CO_2 combining power, particularly if alkali has been used during the theft.

Q. What books do you recommend for the diabetic patient?

DR. EASTLAND: I guess that is directed to me. There are several primers available. One of the old standbys is Dr. Joslin's. Dr. Beardwood has a very good primer, also Dr. Wilder. There is one other if you allow detail men to get into your office. The Eli Lilly people have a book free of charge. It might be doing some advertising but there is a lot of valuable information in it. I believe if all diabetics knew what was in that book it would make it so much easier for the doctor. Do you all have any other book you would like to add to that list?

Q. How do you determine a patient's ideal weight?

DR. DUNCAN: A good plan is to look the patient over and as you evaluate the patient from the general appearance and if he seems to you to be the right weight he probably is. There are so many things that enter into the weight of a person. The big bones, big stature or little bones, little stature, and I go largely by the appearance of the patient. If he appears underweight, then he is below the ideal weight. If he appears overweight, he is too fat. Now, if you want to use the standard weights and take five or ten per cent off that in order to get the ideal weight, for the vast majority of patients you will hit it just about right. The standard average weight is too heavy, but if you use that and take five or ten per cent off, you won't be far astray.

Q. Is there any difference in the therapy of the glycosuria of the chronic fibrotic pancreatitis and true diabetes?

Dr. Beardwood: The question of glycosuria and true diabetes is a simple matter from the diagnostic standpoint if you remember that there are apparently many factors which may produce the clinical picture of diabetes mellitus. If one had a chronic fibrotic pancreatitis, possibly following acute pancreatitis, there may be enough actual mechanical destruction by the fibrous tissue in the islands of Langerhans to produce diabetes. Many cases of diabetes are obviously caused by, or precipitated by, extra pancreatic conditions; the pituitary, the adrenal, and the thyroid may all play a part and also the glucagon or alpha cell secretion may also play a role. All of these conditions develop a true diabetes mellitus. If a patient has glycosuria and no symptoms of diabetes, the differential diagnosis is usually easy by determining the blood sugar value two hours after a heavy meal, at which time one would expect a blood sugar of 110 mgs., according to the Folin-Wu technique. Again if this is equivocal, a three hour glucose tolerance test will usually differentiate diabetes mellitus from renal glycosuria. It is important in doing a glucose tolerance test that the patient be on an adequate carbohydrate intake for at least three or four days before the test is done and also that there is no evidence of acute infection at the time.

Dr. Eastland: In conclusion we have two questions I believe that could be more or less incorporated into one and we are going to aim them over to Dr. Duncan.

Q. Dr. Eastland: The incidence of diabetic neuritis and its management. Please discuss prolonged hypoglycemia and/or cortical damage, differential diagnosis and psychosis, both involving the nervous system. I think I am really giving him a handful.

Dr. Duncan: I'd like to classify the involvement of the nervous system into two groups, the acute peripheral neuritis and the chronic diabetic neuropathies. The peripheral neuritis causes pain; loss of reflexes and atrophy of muscles. That is not very common, neither is it infrequent, and I think the most important thing in the control of this acute peripheral neuritis boils down to control of the diabetes and adequate nutrition. It is very important that those patients should not be subjected to undernutrition when they have a peripheral neuritis because undernutrition makes peripheral neuritis worse. Thirdly, they should be given thiamine chloride in large doses and frequently because it is excreted rather rapidly.

Now, I suspect that the question was really aimed at the much larger group of patients with diabetic neuropathies characterized by numbness or tingling in their toes or feet or legs or fingers, or they may have a little imbalance or staggering when they get to their feet, or they may have nocturnal diarrhea. Impotence is a part of this neuropathic group of disorders.

I want to warn you that most authorities on diabetes disagree with me in the treatment of diabetic neuropathies. What I like to do for these patients is first, and upon this we are all agreed, they should be well nourished. I think that is fundamental.

Nearly all of these patients, their neuropathies get worse if they are allowed to lose weight, but secondly, I use vitamin B_{12}. And I am told that sometime we are going to run across a disorder that won't be cured by vitamin B_{12}, but when a rapid and satisfactory result occurs from the administration of vitamin B_{12} parenterally, it is very gratifying.

Dr. Marble in a Panel on this subject with me, believed that it was due to the control of the diabetes. I agree that the diabetes should be controlled but the response to vitamin B_{12} in the patient in whom it is going to work is rather dramatic after the second or third dose.

In those patients for whom you continue vitamin B_{12} for a long period of time, it is difficult to tell just what caused them to improve, whether control of the diabetes, improved nutrition, or B_{12}. I would make no claim for B_{12} in those that

were stubborn and lasted a long time and then improved, but for those who respond within two or three days, I think that we must give vitamin B_{12} credit until it is proven that it is due to something else.

The dosage that we like is 500 micrograms by injection daily for one week and thereafter once a week until maximum improvement is obtained.

These are very disturbing disorders and they can mimic almost any neurologic disorder. In one case we were both suspicious that the patient had a multiple sclerosis. In another we suspected an intracranial tumor. Each responded promptly to the treatment just outlined. My recommendation would be in these patients, give B_{12} a trial. It will do no harm and, incidentally, it will very shortly establish itself in your mind as an excellent treatment in a fair percentage of these patients.

Now, about prolonged hypoglycemia and cortical damage, that occurs, of course, and it is awfully important that we avoid the risk of prolonged hypoglycemia. My own experience with these patients, and it happens to be two patients, one was my own patient and the other one I saw elsewhere following delivery, and as you may well know, the pregnant diabetic when delivered, we have to be awfully careful of the insulin administration, because at this time these patients are extraordinarily sensitive to insulin. The usual dose of insulin was given to this latter patient and she had a profound hypoglycemia. It didn't last so very long but she complained and still complains of loss of memory. That was about four years ago and she still has very definite impairment in memory. There surely is a real danger of cortical damage in severe, prolonged hypoglycemias and every effort should be made to prevent them.

DR. EASTLAND: I'll now turn the meeting back to Dr. Knotts.

DR. KNOTTS: Time has just about expired and I call your attention to the fact the buffet meal is to be served, and also that the evening session shall start at the appropriate time.

We now adjourn.

THE EFFICACY OF GAMMA GLOBULIN IN THE PREVENTION OF MEASLES*

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Introduction

Following the work of McKhann (1) and his associates (1935) pooled serum from human placentas came into use in attempting to prevent secondary cases of measles in familial groups. This was of limited usefulness due to the development of local and systemic reactions. During World War II there became available quantities of human plasma and fractionation of this by Cohn (2) and his associates (1944) led to the production of gamma globulin. Janeway's (3) work (1944) demonstrated the possibility of modification or protection as objectives obtainable through the selected use of gamma globulin, and in 1945 the Baltimore City Health Department first made available to practicing physicians gamma globulin for family contacts aged six months to three years who had been exposed to measles.

* Submitted June 8, 1955 for publication in the Maryland State Medical Journal.

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[3] Dr. Williams is Commissioner of Health, City of Baltimore.

The work of Christianson and Schmidt (4) of Copenhagen during an epidemic of measles in Southern Greenland in 1951 brought into question, at least in virgin soil, the efficacy of gamma globulin in the prevention of measles. In view of this and the circumstances under which gamma globulin is used in district public health practice, which are not analogous to the somewhat controlled and investigative approach of the original work of Janeway, Professor Philip E. Sartwell of the Johns Hopkins School of Hygiene and Public Health thought that a field investigation was warranted. The personal experiences of the District Health Officer and observations from day to day also had raised some doubts as to whether gamma globulin prevented measles or modified it and a contributing factor in this situation was the wide-spread custom of giving penicillin along with gamma globulin to contacts and also to the original or primary case. These considerations were brought to the attention of the Commissioner of Health who agreed that an evaluation was indicated and participated in the planning of the study which had the following design.

Design of Study

The conduct of a trial of a prophylactic agent whose distribution is determined by well established health department policy must be carried on so that existing regulations are not compromised. Failure to do so could result in criticism that the health of the community was unnecessarily threatened.

Fortunately, it proved possible in the present instance to devise a trial of the efficacy of gamma globulin in the prevention of measles which required no interference with the health department policy of providing biologicals and nursing follow-up to assure that contacts of cases were inoculated with gamma globulin if under three years of age. Previous work by Fales and Top (5) indicated that the measles attack rate among susceptible familial contacts was remarkably constant within the age interval 1–6 years inclusive. The assumption was made then, that among children of this age group, if gamma globulin was not an effective preventive agent, the measles attack rate among inoculated susceptible children (chiefly, under three years of age) would not differ significantly from the attack rate experienced by the non-inoculated susceptible children (1–6 years of age). A further assumption implicit in the study design, was that the extent of exposure of the inoculated and non-inoculated groups did not differ, since all children included in this investigation were familial contacts of proven cases and the families concerned lived under fairly similar housing and cultural circumstances.

Thus this study is concerned with children one to six years of age, living in the Eastern Health District who were familial contacts of cases originally diagnosed by the District Health Officer or by an outpatient hospital physician during the period October, 1953 to June, 1954. In each incident a public health nurse called at the home as soon as possible following receipt of notification of the primary case, to obtain a measles history of each of the household contacts. Inoculation with gamma globulin was suggested for all children below three years of age with no prior history of measles. Follow-up visits were made at about three day intervals and notes made if new cases were observed.

In computing the measles attack rates among exposed children, the following definition was used:

$$\text{Attack rate} = \frac{\text{No. of secondary cases}}{\text{No. of susceptibles}} \times 100$$

Results

A total of 226 children, one to six years of age, was found to have been exposed to a case of measles within the family. Of these 226 children, 131 were inoculated with gamma globulin and 95 were not so inoculated and, therefore, served the function of acting as controls. It will be noted

TABLE I

Secondary Measles Attack Rates in a Susceptible Child Population According to Use of Gamma Globulin

Baltimore, 1953–1954

Treatment Group	Total	Developed Measles	Did Not Develop Measles	Measles Cases Per 100 Children
Total	226	84	142	37.2
Gamma Globulin	131	25	106	19.1
Control	95	59	36	62.1

TABLE II

Secondary Measles Attack Rates in Susceptible Children Inoculated With Gamma Globulin According to Time Interval Between Onset of Primary Case and Inoculation

Baltimore, 1953–1954

Days Between Onset of Primary Case and Inoculation	Number of Children Inoculated	Number Attacked	Number Attacked Per 100 Children
Total	131	25	19.1
0–1	26	2	7.7
2–3	48	6	12.5
4–5	31	6	19.4
6 and over	26	11	42.3

in Table I that there is a striking difference in the attack rate among the inoculated children as compared with the non-inoculated children. Nevertheless, the attack rate among the inoculated children of 19 per cent can hardly be considered to be indicative of a thoroughly effective preventive agent. Therefore, a further study was made of the 131 inoculated children according to the interval which ensued between the day of onset of the primary case in the family and the day of inoculation of the contact child. The results of this study are shown in Table II. The interesting association which is obtained between the protective effect of inoculation and the recency of inoculation relative to exposure is clearly demonstrated. Thus, among children who are inoculated within one day of first exposure the attack rate is reduced to the order of eight per cent as contrasted with the attack rate amongst the non-inoculated children of 62 per cent and with the attack rate of 42 per cent amongst children who were inoculated six or more days following first exposure to a familial case of measles.

Summary

This study, while limited in scope, demonstrated the inherent difficulties in carrying on studies in a service organization and the very considerable extra amount of work done by the public health nurses and the clerical staff in the follow-up of intra-familial contacts. It was noted that most family physicians, if not all, had faith in the ability of gamma globulin to prevent or to modify measles and insofar as prevention is concerned, this study has substantiated that faith. As noted in the introduction, the epidemic in Greenland was in virgin soil and of course this population group cannot be assumed to be immunologically analogous to the population of Baltimore nor can it be assumed that the gamma globulin used in Greenland was the same in antibody content as that used in Baltimore. The study justifies the use of gamma globulin as a matter of official Health Department policy in selected age groups and selected risks.

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in Table I that there is a striking difference in the attack rate among the inoculated children as compared with the non-inoculated children. Nevertheless, the attack rate among the inoculated children of 19 per cent can hardly be considered to be indicative of a thoroughly effective preventive agent. Therefore, a further study was made of the 131 inoculated children according to the interval which ensued between the day of onset of the primary case in the family and the day of inoculation of the contact child. The results of this study are shown in Table II. The interesting association which is obtained between the protective effect of inoculation and the recency of inoculation relative to exposure is clearly demonstrated. Thus, among children who are inoculated within one day of first exposure the attack rate is reduced to the order of eight per cent as contrasted with the attack rate amongst the non-inoculated children of 62 per cent and with the attack rate of 42 per cent amongst children who were inoculated six or more days following first exposure to a familial case of measles.

Summary

This study, while limited in scope, demonstrated the inherent difficulties in carrying on studies in a service organization and the very considerable extra amount of work done by the public health nurses and the clerical staff in the follow-up of intra-familial contacts. It was noted that most family physicians, if not all, had faith in the ability of gamma globulin to prevent or to modify measles and insofar as prevention is concerned, this study has substantiated that faith. As noted in the introduction, the epidemic in Greenland was in virgin soil and of course this population group cannot be assumed to be immunologically analogous to the population of Baltimore nor can it be assumed that the gamma globulin used in Greenland was the same in antibody content as that used in Baltimore. The study justifies the use of gamma globulin as a matter of official Health Department policy in selected age groups and selected risks.

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ASPECTS OF CANCER[1]

PANEL DISCUSSION

MODERATOR: JOHN R. HELLER, JR., M.D.[2]

PANEL MEMBERS: RAYMOND F. KAISER, M.D.
WALTER T. MURPHY, M.D.
STANLEY P. REIMANN, M.D.

ERNEST I. CORNBROOKS, JR., M.D., *presiding*

DR. CORNBROOKS: Ladies and Gentlemen, we are indeed fortunate today to have such a distinguished group to come to us and to talk on this interesting and difficult problem. The Moderator of today's Panel is a man whom most of you know or know of, and, of course, we can say that he lives on Maryland soil, or at least works on Maryland soil. He had a little bit of his training here in Baltimore, which makes us a little bit closer to him and, I hope, he feels a little closer to us. The Panel, today, is going to be on Cancer, and the Moderator will be the man of whom I just spoke, Dr. John R. Heller, Director of the National Cancer Institute in Bethesda.

DR. HELLER, Moderator: Thank you, Dr. Cornbrooks. Ladies and gentlemen, I have always thought that one must have considerable temerity to undertake a general discussion of cancer in the time allotted. I believe, however, that because of the manner in which your committee has arranged the presentations this morning and from what I know of the essayists, you will find this session interesting, helpful and certainly informative.

All of us, have a tendency to think of cancer as a single disease. I have been impressed in the time I have been at the Cancer Institute that we may have to change our thinking considerably and from both the clinical and the research viewpoints; probably we are dealing with as many different diseases in cancer as we have other diseases which confront man.

There are certain similarities in the enzyme patterns which would indicate that cancer tissues tend to converge toward a common type. On the other hand, we have other evidences from the laboratory, that cancers behave quite differently as cancers. We classify cancer by anatomic sites of the body; we classify cancers from the morphologic viewpoint, from their appearance under the microscope. We classify cancers as to their radio-resistance or radio-sensitivity, and there are many other ways of classifying neoplasms which meet the needs of individual circumstances and are utilized by varying specialists and professions. Suffice it to say that the subject of cancer control is preoccupying more and more of the segments of our population and daily we see advances made in the research and control areas.

To help in orienting you for the subsequent discussion, there are several aspects of cancer as a public health problem which I would like to describe. First, there is the rapid rise during this century in the death rate from cancer. Fifty years ago, in the United States, cancer was eighth in the list of causes of death. By 1920 it had climbed to sixth place, by 1940 to second place. Today we find cancer continuing to hold that position, second only to heart disease as a cause of death. This year cancer will take the lives of about 230,000 Americans. In years to come we can expect further increases in the cancer mortality rate. Thus, in looking back over the

[1] Presented at the One Hundred and Fifty-sixth Annual Meeting of the Medical and Chirurgical Faculty of the State of Maryland, on Wednesday morning, April 28, 1954, in Osler Hall, 1211 Cathedral Street, Baltimore 1, Maryland.

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past 50 years, we see that with the decline of the infectious and communicable diseases, cancer has become a national problem, and medical and public health emphasis has shifted to it and to other chronic and degenerative diseases.

There are many reasons for the increase in cancer mortality. Undoubtedly the most important is the changing age composition of our population. Relative to the whole population, the size of the youth group has been decreasing while the size of the older groups has been growing. In 1900 the younger group—those under age 20—represented 44 per cent of the population, while the aged—those over age 55—made up ony 9 per cent. By 1940 the younger group had declined from 44 per cent to 34 per cent of the population. Persons over 55 had increased from 9 to 15 per cent of the population. The total population of the United States continues to increase and so does the proportion of persons in the older age groups. These increases are expected to continue, so that the population trend alone will greatly increase the magnitude of the cancer problem in this country.

Generally speaking, illness from cancer increases very rapidly during adult life and old age. This was brought out by some of the findings in the National Cancer Institute's survey of cancer morbidity in 10 metropolitan areas in 1947. Among the residents of these areas the incidence rate for cancer at age 25 was about 40 per 100,000, at age 50 about 475 per 100,000, at age 75 about 1,900 per 100,000 of population. There is an interesting exception to this trend. It is that although cancer morbidity and mortality generally increase with age, there is a reversal of the trend during the early years of life. The cancer illness rates are higher for children under 5 years of age than for children between the ages of 5 and 15 years.

Cancer is being found as frequently in males as in females, but the survival rate is considerably lower among the males. The main reason for this is that a larger proportion of cancers in males are those which originate in inaccessible sites—such as the stomach and the lungs—and which have a poor prognosis. From age 10 to about age 60, the incidence of cancer is greater among females. From age 60 onward it is higher for men.

We are inclined to emphasize the increase in cancer illness at the older ages, and this is natural, because the rates at the older ages are high. However, when we think in terms of actual numbers of new cases, we must not overlook the very substantial number among children and young adults. Roughly one of six newly diagnosed cases of cancer is in persons under 45 years of age.

While the incidence of cancer is essentially the same in the two sexes, there is a marked difference in the distribution of cancers by site of origin. One of the most noticeable differences is shown by cancer of the respiratory system. Twelve per cent of cancers in males originate in the respiratory system, but only 3 per cent of the cancers in females start there. The increase of this form of cancer in white males during recent years has been alarming. Since 1914 the picture for death rates for respiratory diseases among white males has changed radically. Influenza, pneumonia, and tuberculosis have declined steadily as causes of death, while the death rate from lung cancer has climbed rapidly. Today the lung cancer death rate among white males is something on the order of 25 times greater than it was 40 years ago. The lung cancer picture for women is not as dark as that for men. The rate for lung cancer mortality for women has gone up since 1914, but it has not kept pace with the rate for men. In fact, lung cancer does not approach some other types of cancer as a cause of death in women.

I shall not go into a discussion of cigarette smoking or other factors which have been suggested as causal influences in lung cancer. Suffice it to say there seem to be a multiplicity of factors which play a part in the production of cancer of the lung. All the data we are able to get indicate that an actual increase in the amount of lung cancer in our population is occurring, that it is an

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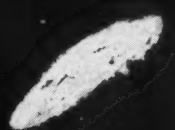

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alarming increase, one which cannot be explained away by attributing it to better reporting and improved diagnosis. The ultimate solution to the lung cancer problem lies, I think, in preventive measures.

It may be interesting to look at the mortality trends since 1914 for other leading forms of cancer in white males. A slight downward trend has developed for cancer of the prostate, although it may not be of much statistical significance. Little change appeared for cancer of the stomach until 1930. Since then it has declined noticeably as a cause of death. The rate for cancer of the intestine shows little change, however. As a cause of death, the gastrointestinal cancers taken as a group have shown slight change during the last 10 years. This would mean that with refinements in surgery, better diagnosis, and earlier recognition, we are beginning to achieve reasonably good management of gastrointestinal cancer. This is reflected even more noticeably in the declining death rate for cancer of the stomach in women.

For white women the death rate from breast cancer has come down sharply as has the rate for cancer of the uterus. Obviously, these declines are a reflection of better management. Despite the fact that carcinoma-in-situ seems to be on the increase, it would appear that some of the most hopeful opportunities for the prevention and management of cervical cancer lie in the area of pre-invasive cancer.

The morbidity and mortality trends among Negroes differ in several respects from those among whites. For example, the per cent of deaths due to stomach cancer is greater among Negro males than in white males. Lung cancer, however, is less frequent among Negro males. Cervical cancer is much more frequent in Negro women than in white women. Of all the racial groups in the United States, Negro women have the highest incidence of cervical cancer.

If one were to take up the major sites of cancer and analyze each site from the standpoints of prevention and medical management, one would find it quite productive of discussion. Since we will not undertake that analysis this morning, perhaps we should turn to the members of the panel and hear what they have to offer us.

The panel consists of Dr. Raymond F. Kaiser, Dr. Walter T. Murphy, and Dr. Stanley P. Reimann. Dr. Kaiser is the Chief of the Field Investigations and Demonstrations Branch of the National Cancer Institute. This is our Control Branch through which the findings of research are passed on to the field to benefit the cancer patient and the private physician.

Dr. Murphy is Chief of Therapeutic Radiology at the Roswell Park Memorial Institute in Buffalo, New York. Dr. Murphy will discuss some of the elements which are important in the therapeutic management of cancer from the standpoint of radiation. Dr. Reimann, a pathologist and longtime friend of ours, is Director of the Philadelphia Institute for Cancer Research and certainly is competent and qualified to discuss the field of cancer research.

The first essayist this morning is Dr. Kaiser, who will point out some of the salient facets of cancer control.

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COMMENTS ON CANCER CONTROL PROGRAM

RAYMOND F. KAISER, M.D.*

Cancer control is concerned with the actual prevention of cancer whenever possible, with the discovery of the disease in its earliest stage and with the provision of adequate services and facilities for diagnosis and treatment. Ideally, a cancer control program to be effective requires:

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1. An alert and trained profession.
2. An informed public.
3. Suitable methods for prevention of the disease.
4. Case finding, screening or diagnostic procedures which can be applied on a mass basis to sort out those individuals with the disease from the remainder of the population.
5. Adequate services and facilities for diagnosis and treatment.

The cancer control program of the National Cancer Institute is designed to meet some of the needs which exist in these requirements, and to demonstrate appropriate methods for fulfilling some of these conditions. This program, which is now in its eighth year, has special implications for practicing physicians.

Cancer diagnosis and treatment frequently call for the services not of a single physician, but of a qualified team. However, the cancer patient is ordinarily seen first by a general practitioner, and it is his diagnostic training and experience that often determines the outcome. For this reason the major emphasis in cancer control is on programs designed to aid the physician—programs to improve professional education at the undergraduate, graduate and postgraduate level, and to provide diagnostic and other special services to help the physician do the most effective job.

If the physician is to successfully manage an optimal number of cancer cases, he must bring to his practice an awareness of cancer in all of its diverse manifestations. Obviously the place to inculcate such an awareness is in the undergraduate school, however, I think it can be fairly said that until a few years ago most medical school curricula did not provide an effective and integrated presentation of this important subject. On the basis of a study of cancer teaching in medical schools made early in 1946, our National Advisory Cancer Council recommended that the National Cancer Institute undertake a program of financial assistance to medical schools to coordinate and improve the teaching of cancer to undergraduates, thereby increasing the students' awareness of cancer. The program, based on these recommendations, has gained universal acceptance during the seven years of its operation and today all approved medical schools are participating in the program. Each of the 4-year medical schools receives a grant up to $25,000 annually, and each 2-year medical school receives a grant up to $5,000 a year for the broad purpose of correlating and improving its cancer instruction. Within this general purpose the schools have been permitted maximum latitude to develop the type of program which best meets their particular circumstances. We have always felt that direction of teaching programs must not come from the outside but must be intramural and autonomous. Our belief has been justified not only by the widespread acceptance of this program, but by the perceptible improvement in cancer teaching.

A parellel program through which grants up to $5,000 annually are made to dental schools for instruction of undergraduate students in the recognition of oral cancer has been in existence for approximately the same period of time. This program is based on the fact that a large proportion of oral cancer cases are first seen by dentists and only a limited percentage of these are recognized as malignant conditions requiring immediate referral to adequate medical attention. This program, too, has enjoyed widespread acceptance and practically all approved dental schools are participating.

In recent years considerable effort has been devoted to the improvement of cancer instruction in a limited number of schools of nursing in order to determine the most practical methods of providing recent graduates with a better understanding of cancer and to better equip them to handle cancer nursing activities.

For a number of years similar educational grants have been extended to a small number of Schools of Public Health in order to provide instruction for health department personnel in the public health aspects of the cancer problem.

With the increase in the magnitude of the cancer problem there has developed a need for

physicians with special training in the diagnosis and treatment of cancer. Both voluntary and governmental groups provide support for specialized training of graduate physicians. The Institute's program enables young graduate physicians interested in cancer to undertake clinical training in specialized fields related to its diagnosis and treatment. Over the recent years there has been a sharp increase in the number of physicians receiving such training in the three major disciplines of surgery, radiology, and pathology. At present there are 143 graduate physicians being supported in such training throughout the country.

For the practicing physicians there have been a number of attempts made to bring recent information about the disease directly to them. One of the most important of these has been the production, jointly by the Institute and the American Cancer Society, of a series of films for professional audiences depicting the early diagnosis of cancer. In this series there have been individual films dealing with the diagnosis of breast, gastro-intestinal, uterine and oral cancer. There is currently in production another, which will be released this year, dealing with the diagnostic aspects of lung cancer. These films have been made available to practitioners through medical societies, medical schools, State health departments, and State divisions of the American Cancer Society.

Other attempts at professional education have been handled through support of National cancer conferences, cancer symposia, professional bulletins, cancer manuals or guidebooks, tissue slide loan services, and refresher courses. These attempts at professional education have met with varying degrees of success, however, it is an essential part of the cancer problem and is considered a field requiring continuous efforts.

An Informed Public

The history of public understanding of the cancer problem in America has been one of gradual gain in the past century, with a marked increase in public interest and awareness of cancer in recent years. It is conceded by most authorities that a large continuous educational program, based on accurate data and utilizing currently available knowledge, will result in considerable control of mortality from many types of cancer. To be successful, a public educational program must be such that it will stimulate the individual's awareness of cancer and motivate him or her to seek medical attention at the earliest possible moment in the development of cancer.

Toward this end, that is, an informed public, the Institute has developed educational materials which complement those of voluntary groups, and has produced, in conjunction with the American Cancer Society, public informational materials notable among which has been the film "Breast Self-examination" which presents to women basic facts about breast cancer and urges them to seek consultation with their physicians at an early date. Another recently released film, "The Warning Shadow," was produced under the same sponsorship and is directed toward males over 45 years of age, urging them to seek semi-annual chest x-rays from their physicians.

In addition to the actual assistance in production, the Institute has developed arrangements with the American Cancer Society which assist in the utilization of such informational material in a manner which would stimulate the individual awareness of cancer and motivate the early seeking of medical care.

In general, the public is better informed about cancer today than at any time in history, however, even with progress in research and therapy, the educational problem will continue and, in fact, will be increased automatically.

Cancer Prevention

In the field of cancer prevention, knowledge has been meager largely because in the past cancer workers have given little attention to environmental factors which may have a rela-

tionship to the causation of human cancer. Much of the knowledge now available has resulted from studies on small groups of people utilizing statistical, genetic, epidemiological, and other techniques to uncover relationships between cancer and environmental factors. For example, the first known etiological agent for scrotal cancer was confined to a small occupational group, the chimney sweeps of London.

Since the inception of the cancer control program the potentials lying in the field of environmental cancer have been recognized and it was felt that if relationships could be established between certain specific materials the individual encounters in his home and industrial environment and the development of cancer, it would be possible to eliminate or reduce the exposure to such carcinogenic materials, thereby preventing the development of certain cancers.

Numerous studies and investigations have been undertaken directly or have been supported through grants which have an immediate bearing on environmental factors. Out of these has come the recognition that the problem of carcinogens has become one of environmental agents involving, in many instances, many, if not all, persons in modern populations. In addition, it is evidently essential that the tissue be exposed to these agents over a long period of time, thereby presenting a long latent period before specific cancers appear.

While there is much disagreement regarding the exact nature and the role of some of these so-called environmental carcinogenic factors and, I need mention here only briefly, the current controversy concerning the relationship of cigarette smoking and lung cancer, there has been accumulating in recent years much evidence that cannot be overlooked in respect to cancer control activities.

Among the environmental factors that have been shown to be carcinogenic are: (1) certain products and by-products of the manufacture or processing of aniline dyes, coal tars and petroleum, (2) arsenicals and some inorganic chemicals, and (3) radioactive substances, x-radiation and ultra-violet radiation. As more is learned about these and other suspected carcinogenic agents it is feasible to consider the establishment of cancer prevention programs in locations where such hazards exist, incorporating safe production and handling methods for the hazardous materials and instituting periodic examination of the exposed workers.

This is an aspect of the cancer problem which has come under systematic study only recently and in which increased efforts offer unlimited possibilities for making significant contributions to the solution of the cancer problem.

Diagnostic Tests and Case Finding

The key to cancer control today is early diagnosis and treatment, but this statement points up one of our biggest problems—how to find the cancer case early enough. It is recognized that there is no method available today other than general periodic physical examinations which holds promise of discovering early cancer of all types in the population. Periodic examinations do provide the opportunity for discovery of a sizeable number of early lesions since more than one-half of all cancers occur in sites accessible to direct examination. However, this method is expensive and time consuming; and even if all persons of so-called cancer age could be persuaded to seek periodic examination, there are simply not enough trained hands in the country to do the job. There is an urgent need, therefore, for a type of test which can be applied on a mass basis at reasonable cost and with sufficient specificity that it will identify a high percentage of cancer cases in an early stage.

For a great many years laboratory investigators as well as practicing physicians have been looking for differences between persons with early cancer and cancer-free individuals—subtle differences in the blood, sputum, urine and various body chemicals. The belief that these differences are specific and measurable forms the basis for many reported so-called diagnostic

tests. There have been numerous attempts to develop diagnostic and screening tests, and more recently, the entire subject has aroused great public and professional interest. The demand for a diagnostic test has become so great that every new procedure that is proposed is in danger of premature exploitation before its clinical validity can be determined. Recognizing this situation, the Institute, through its cancer control branch, established a cooperative program with investigators in a number of medical schools under which evaluation of reported cancer tests is carried out under controlled conditions. At the same time, other investigators are encouraged, through grants, to pursue new leads which show promise for the development of a diagnostic or screening test.

Although there is not available a general diagnostic test for cancer, there have been developments in recent years in the search for diagnostic tools which may form the basis for a screening test for cancer of specific sites. One of these, the cytologic method developed by Papanicolaou and Traut for the discovery of early cervical cancer, has been evaluated and promoted as a diagnostic aid. Its usefulness as a screening procedure for uterine cancer is currently being evaluated by the Institute in a study being conducted in Memphis and Shelby County, Tennessee in cooperation with the University of Tennessee Medical School and the County Health Department. The original cytologic technique has been modified for use in the discovery of cancers of other sites; namely, lung, prostate, gastric and bladder cancer, however, its usefulness and feasibility in these types of cancer have not yet been fully evaluated either as a diagnostic or screening procedure.

A recent development in this field which shows promise is the test for prostatic cancer, developed by Fishman and later modified by Cline, both of which developments were supported through the Institute's control program. Here again further evaluation is necessary and is being carried out by the Institute.

Even more recently Penn and Dowdy, with partial support from the control program, have developed a simple blood test which shows some promise of being able to distinguish between people free of cancer and those who may have it. *Much* more work and evaluation must be carried out on this procedure before it can be declared acceptable.

It might be appropriate at this time to clarify the type of test in which cancer control workers are most interested. Primarily, it is a test which will separate a large group of examinees into two categories—one consisting of those whose reaction to the test is negative, and the other consisting of a relatively smaller number of persons whose reactions are positive and who are, therefore, cancer suspects. It should be a test which would pick up a high percentage of individuals with early localized cancer. It should have a high degree of specificity without a large percentage of either false negative or false positive results. If an acceptable test which meets these general criteria can be developed, it would be a significant forward step in cancer. While such a test would not eliminate the need for carrying out further diagnostic producers to diagnose the case, it would make it possible to concentrate diagnostic efforts on the small group of individuals with positive test results. Despite the many problems associated with the development of an acceptable mass screening test, results to date have been encouraging and it seems entirely possible that a test or battery of tests can be developed which will be effective on a mass screening basis in sorting out cancerous and non-cancerous individuals.

In this connection, a small beginning has been made to conduct and support studies of a statistical, epidemiologic nature which might reflect geographic, climatic, racial, socio-economic and environmental differences in the occurrence of cancer. Preliminary data from some of these studies suggests that it may be possible to sort out the kinds and types of people who would be most apt to develop cancer. If such determinations could be substantiated it would

make it possible to more appropriately direct case-finding efforts toward groups with the promise of the greatest cancer yield.

Cancer Facilities and Services

One of the most practical activities which has contributed to the control of cancer to date has been the organization and operation of cancer clinics. Such clinics, usually operated in a general hospital, provide an environment in which representatives of the various specialty groups concerned with cancer, such as surgery, pathology, radiology, etc., can work with the patient's physician in arriving at an accurate diagnosis and effective treatment. The number of cancer clinics in the nation has increased markedly in recent years. However, there are still fewer than required to meet the need and the establishment of additional cancer clinics is being promoted and encouraged. This, along with various other types of services for physicians, has been encouraged through the Institute's program of grants to State Health Agencies for cancer control activities.

Under this program, each State receives an annual allotment based on a formula which takes into account cancer mortality, financial need, extent of the problem, and population density. The grants are required to be matched on a two-for-one basis. These funds may be used for a variety of purposes which aid physicians as well as the cancer patient. Included among these are support for cancer clinics, cytology services, tissue services, cancer registers, statistical research, professional and lay education, nursing services, limited hospitalization for diagnostic purposes, tumor registers, environmental cancer programs and tissue slide loan registers. All of the official State agencies now have cancer control programs incorporating a few or several of these features.

Conclusion

An extensive, dynamic cancer control program is underway in this country. It has resulted from the combined efforts of many professional groups, private, voluntary and governmental, as well as the efforts of medical specialists, clinicians, private practitioners, public health workers and scientists. There is a continuing need to improve the nature and effectiveness of the program. The latter will improve as cancer research provides more knowledge about the carcinogenic process with regard to diagnosis, treatment and prevention.

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RECENT TRENDS IN THERAPEUTIC RADIOLOGY

WALTER T. MURPHY, M.D.*

It is a little more than half a century since the first clinical application of radiation was made. During these relatively few years therapeutic radiology has evolved from trial and error methods to its present scientific stage. This has been facilitated by accurate observations by both radiologists and allied scientists of experiments on animals and the clinical study of humans following accidental and purposeful exposures to sources of radiant energy.

Occasionally it is rewarding to stop and think of the great strides that have been made in the clinical application of a modality whose major biologic effect is destruction. It is to the credit of the many early pioneers and to the investigative and clinical scientists of today that such

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destructive forces may be harnessed in a manner that can cure as well as palliate human cancer patients.

In our enthusiasm, however, for the newer super-voltage and better-publicized radiological instruments, it is most imperative that the tried and true instruments and methods are not wholly discarded without scientific reasons.

One should digest carefully the clinical claims made for any new method or radiation source. It is quite often that one reads or hears of spectacular cancer results that are based upon a few months post-treatment observations. Many times comparable immediate results have been possible with conventional equipment and methods. Much of the so-called conventional equipment has been improved not only as far as the x-ray tube is concerned but also in its tube stand or mounting. A beryllium window in an x-ray tube allows the transmission of very long wave length radiation which may be utilized successfully in the treatment of superficial cancers. Moderately high voltage in a small sized unit is possible because of revolutionary advances in transformer and tube design along with gas insulating systems. Newer developments in the tube carriage permits not only flexibility for stationary fields but also for moving beam therapy (rotation, pendulum, converging, etc.)

It is most important that the investigative and clinical aspects of radiation therapy are encouraged to progress. Expensive equipment, if proved superior, should be made available to any cancer patient who needs it. That life is very precious to the patient.

It is pertinent here to point out that the most common and accessible radiation therapy machines and radium sources are not always used in a way that would be best for a patient. The skill and conscientious efforts of the radiation therapist are and always will be more important than the limitations of his radiological equipment. It is just as sane to remark the obvious—that the combinations of skill, conscientious effort and adequate instrumentation will add up to a total of excellence which must result in more cancer cures with less biological complications.

When it is clinically obvious that neither cure nor palliation is possible, any application of radiation is merely prostituting the specialty of radiology. All clinicians should recognize this and refrain from using radiation as a "placebo." In investigative centers it is sometimes necessary to try newer instruments and technics on the obviously hopeless cancer patient. In these instances the procedures are well controlled and administered, and from these clinical trials, much useful information, as well as notable advances in palliative procedure have been forthcoming.

Trends in radiation therapy must be catalogued under several topics, since both the science of medicine and the basic sciences are involved. At the same time any scientific appraisal and decisions should be tempered by common sense and appreciation of the humanities.

The most noteworthy advance is the better training of the radiological resident and the availability of better post-resident experience. The new therapist today has a much better understanding of the physical-chemical foundations of radiology than the trainees many years ago. This is not only because of the basic information that is available today but is also due to the training programs which therapeutic centers are able to provide. In their quest of knowledge concerning the physical foundations of radiology, it is most important that these same candidates do not disregard the importance of clinical acumen which in this case could be defined as the appreciation of the relative importance of organ systems as related to the entire human being. It is already too true that sometimes the therapeutic procedure is so directed to a cancer site that the so-called tumor dose in roentgens tends to be more important to the therapist than the eventual welfare of the patient.

Now that radioactive isotopes are being so widely used both as diagnostic as well as therapeutic agents, the therapist has not only the

welfare of the patient to consider, but the health of the whole community. This is necessitated by the fact that many radioactive isotopes, after application in the body, are stored and released from the body in different manners and in different proportions of radioactivity, which could create dangers to the health of not only the professional attendants, but through the water supply, etc. to the entire community. For these and other reasons, proper and adequate training and experience are necessary before permitting one to use radioactive isotopes. Experience and innate ability will nurture the background of physics, etc. so that the therapist will be able to best utilize his radiation sources.

Recently there has been an international attempt to standardize depth dose data as well as methods used in the measurement of dose rates. It has been needed for a long time because of the variations in different radio-therapeutic centers.

The well known quantitative terms "r" (roentgen—for x-ray and gamma radiation) and rep (roentgen equivalent physical—for beta radiation) have not adequately expressed the true "tissue dose." Therefore, the term "rad" has been recently adopted. This "rad" means an amount of energy absorbed, namely, 100 ergs per gram of irradiated material.

Any possible success with radiation therapy depends upon a safe ratio or differential between the cancericidal dose and the accompanying normal tissue dose. This premise is the driving motive for better technics. One must consider: (1) The site and extension of the cancer. What modality and/or quality of radiation would best be indicated? (2) What is the minimum total amount of radiation in physical dosage within an optimum period of time that could destroy all the cancer without creating a normal tissue or whole body reaction or impairment that would be unendurable by the patient or fatal to the patient? (3) How would this dose be applied? Here, the number, size and positions of external radiation ports would be considered as well as type, strength and number of intra-cavitary, interstitial or whole body radiation sources. One must consider what daily dose to the cancer site would be optimum and best tolerated by the normal structures.

From these questions it is obvious that, while a great many cancers may be easily, adequately, and safely irradiated, there are other cancers where it is difficult or impossible to secure good results with equipment and technics formerly available. The most common difficulty is that many cancers are situated deeply in the body or are encompassed wholly or partly by bone. In these instances, it is necessary to utilize a radiation source that can penetrate to the cancer site without having its energy depreciated too much by intervening bone and soft structures. This necessitates the utilization of hard penetrating radiation.

It is also important that this radiation beam be as straight and as uniform across its width as possible—Figure 1. The intensity of the radiation in the center of a radiation beam may be much greater than at the edge which might leave the periphery of the cancer underdosed. As the quality or hardness of the beam increases, the isodose planes flatten out so that the intensity at the edge more nearly approximates that of the center.

It is a physical fact that the energy absorption of radiation in bone is dependent upon the quality of that radiation. With qualities of radiation up to H.V.L. 0.5 mm. Cu. (140 K.V.P. + filter of 0.25 mm. Cu. and 1.0 mm. Al.), energy absorption in bone increases, whereas after this quality the energy absorption in bone decreases.

It is sometimes practical to take advantage of such bone absorption factor in the treatment of a skin cancer invading bone and cartilage. Figure 2 shows a patient with a squamous cell carcinoma of the skin involving both cheeks, medial canthus of each eye and invading the nasal passage with destruction of the nasal bone. In this case the use of an x-ray quality of H.V.L. 0.5 mm. Cu. (140 K.V.P. + 0.25 mm. Cu. and 1.0 mm. Al. filter)

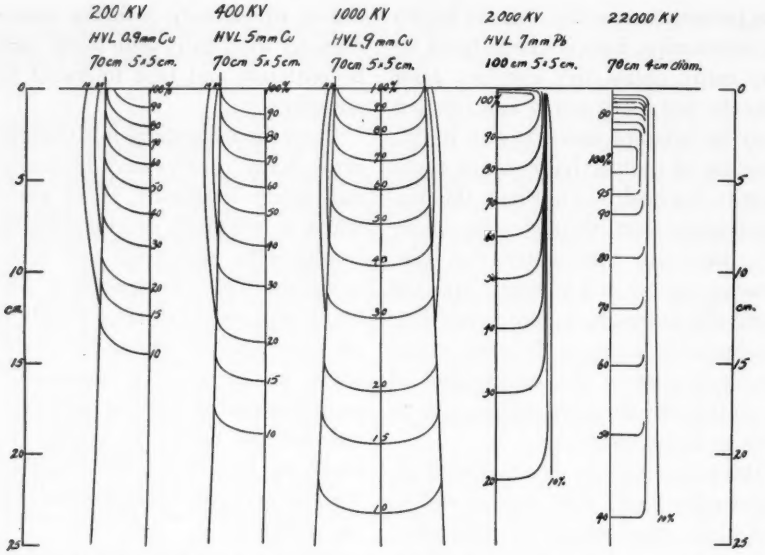

FIG. 1. Isodose curves for x-rays from 200 K.V.P. to 22,000 K.V.P. With increase in hardness, the x-ray beam attains a greater depth intensity with more uniform width and with less lateral or backscatter.

allowed the maximum bone absorption in order to give adequate irradiation to the cancer cells in the bone, adequate penetration to irradiate the nasal passages and ethmoid area, while at the same time made it practical to adequately protect the eyes by lead shields from the irradiation.

At Half Value Layers of 3.0 mm. Pb. (1000 K.V.P.) and harder, or, with Cobalt-60 and radium, the absorption in soft tissue and bone approximate one another. Along with this behavior, the electronic equilibrium of the radiation beam takes place under the surface of the skin. With qualities of radiation emerging from a Betatron and Synchrotron (24 Mev. and up)[1] the intensity of the radiation at a point 5 cm. under the surface of entry may be 60% more than the energy absorption on the surface. The practical application of this physical fact is apparent. One may deliver to anatomical depth points large amounts of radiation energy with less skin surface or bone absorption than would occur with softer radiation (e.g. 140 K.V.P. (H.V.L. 0.5 mm. Cu.) to 250 K.V.P. (H.V.L. 2.5 mm. Cu.)). At the same time, the amount of radiation leaving an anatomical site is great, which fact necessitates care in estimating exact contributions to exit portals.

The advantages of radiation of 1000 K.V.P. x-ray machines and up or radium and Cobalt-60 sources may be listed as follows:

1. Greater penetration and hence better depth dose.
2. Better beam definition and uniformity.
3. Energy absorption in bone and soft tissue is closely similar.
4. Less volume or integral dose—less radiation sickness.
5. Skin reaction is not a limiting factor to depth dose.

Since the mild biological changes in the skin might delude the uninformed observer into a state of complacency, it is important to realize that the effect of such increased depth intensities must be a first consideration. It is not necessarily true that the greater the dose delivered, the better will be the result. The increased depth dose might be more cancericidal, but it might at the same time create such irreversible effects

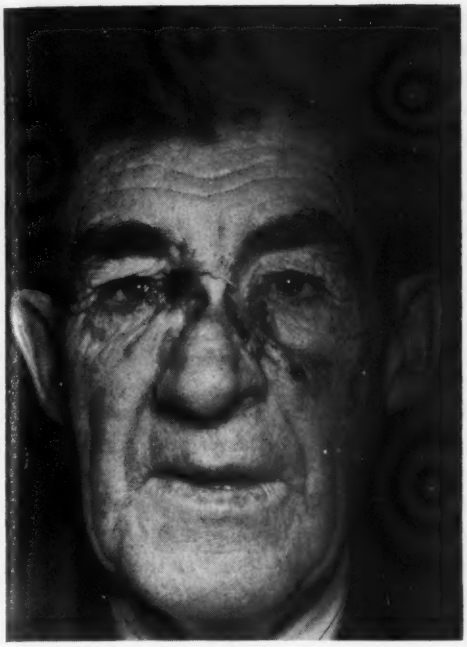

FIG. 2A

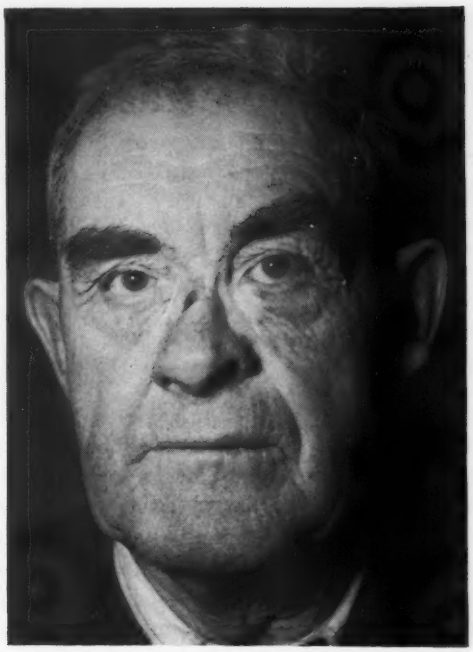

FIG. 2B

FIG. 2. This illustrates results that are attainable with a conventional low voltage x-ray machine.

A. Before treatment. H.V.L. 0.5 mm. Cu. Rt. cheek-nose-canthus port 5½ x 5 cm., Left port—8 x 7 cm., S.T.D.—18 cm., Daily increment 300 r. Total Surface Dose to each port—5400 r.

Depth Dose at 1 cm.—Right port—4428 r.
Left port—4487 r.
at 2 cm.—Right port—3624 r.
Left port—3747 r.

Overall Treatment Time—26 Days

B. 3 yrs. and 9 months after treatment—No clinical evidence of cancer.

upon the contiguous normal tissue bed or organ system that unendurable tissue changes or death would result.

With the qualities of radiation delivered by a betatron or synchrotron, co-axial entrance ports or other multiple port arrangements are not always practical. Here, many cases must be treated through a single port, utilizing the fact that such beams at certain areas of depth (e.g. 3 to 6 cm.) might be approximately 60% more energizing than at the surface. However, with beams of radiation in the range of 400 to 2000 K.V.P. x-rays or gamma radiation from radium or Cobalt-60 sources, multiple stationary port settings or rotational methods are necessary to deliver optimum depth dosage. Recent years have seen the popularization of careful multiple port planning as well as rotational and scanning technics. With these methods, the tumor dose is delivered through multiple entrances and pathways which spares the normal tissues while allowing much greater tumor doses.

Fractionation of the total dose over a period of many days or a few weeks also permits higher total tumor doses. When this fractionation with multiple daily doses is applied so that several ports of entry are treated each day with small increments instead of one port each day with a large increment, the effect upon the skin and

CHART 1

Late Bladder and/or Rectal Reactions

Cervix cases 1941–1946

H. V. L.	Total Number Cases	Number Reactions	% Reactions
0.9 mm. Cu. (200 K.V.P.).....	399	27	6.8
5.0 mm. Cu. (400 K.V.P.).....	67	7	10.4
9.0 mm. Cu. (1000 K.V.P.)....	145	24	16.5
Total	611	58	9.5

Five year N.E.D. Rate of the *58* cases was 75.8%.

Five year N.E.D. Rate of all cervix patients during the same period was 39.6%.

subcutaneous tissue is much more tolerable.[2] This may be illustrated by cervix patients treated through four converging pelvic ports. Should each of the four skin ports receive 125 r.* each day for a total dose to each skin surface of 4500 r. within six weeks, the late skin and subcutaneous changes would be very mild (slight atrophy, temporary epilation and very minimal subcutaneous fibrosis). However, should in the same patient, only one of four successive ports be treated each day with 500 r. within the same period of time and for the same total skin dose, the late changes would be severe (scarring, epilation, telangiectasis and marked subcutaneous fibrosis). Comparable relative changes would accompany groups treated with 100 r. to 4 ports vs 400 r. to one of 4 ports daily, and 150 r. to 4 ports vs 600 r. to one of 4 ports daily.

It has also been apparent that in the treatment of superficial lesions through one port (e.g. skin cancer), that fractionation of the dose minimizes the occurrence of late inflammatory breakdowns at the site of the treatment. This knowledge has lead to the abandonment of massive dose technics in the treatment of skin and lip cancer (e.g. 1000 r. × 5 or 1500 r. × 3, etc.). Instead, today, the greatest increment is 500 r. (e.g. 500 r. × 8 or 9) for small lesions. The majority of lesions receive 400 r. × 13 to 15 or 300 r. × 18 to 20 given daily.

There has been a general trend to more individualization of irradiation. The therapist realized that he must be first a clinician and examine each patient together with a review of all pertinent laboratory or other investigative findings. Following this, he can better plot out a method of attack.[3] Usually life size anatomical contour drawings are made at the cancer level. By manipulating isodose charts over this patient outline, the percentages of the surface dose which reach the cancer sites as well as the normal organs are recorded. Summation isodose curves may be made in addition to adding up the contribution of each port to any anatomical point. The final technical diagram is recorded on suitable clinical treatment forms and outlined on the skin of the patient or a plaster cast which may be placed on the patient previous to each treatment. Again it must be said that there are limits of dosage beyond which end results get worse. A few years ago it was found at the Roswell Park Memorial Institute that total tumor doses delivered to the uterine-parametrial area by x-ray and gamma radiation over the aggregate of 9000 r. within 4–6 weeks (depending upon proportion of x-ray "r" and gamma "r") resulted in fewer five year apparent cures. Comparable lessons regarding tolerable doses have been learned from the irradiation of other intra-abdominal, pelvic and chest cancers.

Increase in depth dose resulting from the use of hard radiation (high voltage, etc.) is usually accompanied by a rise in radiation complications. This is clearly shown in Chart 1 which records the incidence of bladder and rectal complications in a series of cervix cancer patients, all of whom received radium applications to the uterine canal and face of cervix, as well as the external x-ray treatments. It is seen that the complications increase with the increase in hardness of the x-ray beam. It is also noted that the five year apparent cure rate in these cases was 75.8%. This was higher than the no evidence of disease rate of the entire cervix group during the same period 39.6%.

Advances in physical knowledge and engineering have resulted in generators and port designs

* All Roentgen doses are tissue doses.

FIG. 3A

FIG. 3B

FIG. 3. Carcinoma of the Prostate—Metastatic to bones.

A. Before treatment (Pituitary—adrenal irradiation, stilbestrol medication and orchiectomy were all inaugurated concurrently).

B. Four years after treatment. Almost complete disappearance of metastases.

that allow the clinical utilization of the electron beam. Its peculiarities permit confined irradiation. Widespread skin lesions such as mycosis fungoides have been successfully palliated by an electron beam from a 2000 K.V. Van de Graaff machine.[4] The electron beam from a linear accelerator operating at 14 MEV (and higher) would penetrate into the tissue to a depth depending upon the energy and would have a sudden "fall off" in the depth beyond which no appreciable irradiation effect would take place. Although such equipment is very scarce the possibilities for clinical application are apparent.

The opportunity of selecting a quality of radiation that is tailored for the individual clinical problem and the application of careful treatment planning utilizing multiple or infinite portal technics, have opened more hopeful fields for the radiation therapist. There has been renewed interest in the treatment of lesions of the brain, pituitary gland, oral-, naso- and laryngeal pharynx, larynx, breast, esophagus, lung, urinary bladder and uterus. In order to alter the hormonal influence upon cancer cells, irradiation of endocrine glands has proved efficacious in certain cases. X-ray therapy directed to the pituitary[5] and adrenal glands has created remissions in some metastatic prostatic cancer patients who were in relapse following orchidectomy and stilbestrol medication. In certain cases such irradiation has obviously enhanced the effect of orchidectomy and stilbestrol as seen in Figure 3.

Probably the most spectacular trend in recent years has been in the utilization of radioactive isotopes. As far as cancer therapy goes, however, their accomplishments do not match their diagnostic and investigative importance.

Cobalt-60 has proved a good substitute for radium sources with its own advantages and disadvantages. The former might include its lower cost, its monochromatic gamma radiation and its very low-energy beta radiation which is more easily screened out than the beta ray of radium. Cobalt is solid, relatively unbreakable, magnetic and may be machined to various shapes and sizes before being made radioactive. At a suitable time during its life (half life 5.3 years) it may be "reactivated." It does not generate any radioactive gas and has a greater flexibility and accuracy in the physical planning of treatment. Its main disadvantage is its relatively short half life. Although its immediate cost is much cheaper

than radium for unit strength, the ultimate long time cost would be markedly increased due to reactivating expense.

Iodine-131 is most effective in those metastatic thyroid cancers which show a histologically differentiated, follicular, colloid-forming structure. Surgery and conventional irradiation remain the best treatment for the primary tumor site. The uptake of I-131 in these metastatic lesions may be enhanced by removing the thyroid gland or decreasing its function by administering anti-thyroid drugs and I-131. It is one instance where a specific therapeutic agent is indicated, since no other form of treatment can accomplish what I-131 can in those 10–20% of metastatic thyroid cancers that will "take up" suitable amounts of this radioisotope.[6]

Phosphorous-32 is the treatment of choice for polycythemia vera, and is a valuable tool in the management of chronic myelogenous leukemia, although in the latter it does not necessarily surpass conventional x-ray treatment.

Gold-198 may be used in a colloidal form in the palliation of some pleural and peritoneal serosal effusions due to cancer. It is now being investigated in wire or seed forms for its interstitial effect upon tumor sites.

There are others, such as Yttrium-90, which because of their own peculiar radioactivity may prove useful clinically.

It is fervently hoped that in the future a labeled radioactive organic compound will be found that, like I-131 in thyroid cancer, will be specific for other types of cancers and their metastases.

Since all ionizing radiations are destructive to a degree, it is well to devote a final few words to the possible sequelae of such radiations. It is the aim of every alert radiation therapist to recognize the hazards of radiation, detect and avoid unnecessary exposure and to insure maximum protection for unavoidable exposure. However, certain tissue changes are inevitable especially with cancericidal irradiation.[7] With modern and still improving technics, tissue changes such as radiation dermatitis, bone necrosis and bowel ulceration are being kept to a minimum. However, in a conscientious effort to eradicate a cancer, the clinician must consider not only whether such sequelae are possible but whether they are probable. The carcinogenesis of radiation is a limiting factor in the determination of safe dosage. This is not only true of externally applied radiation but also of long-lived isotopes.

From animal experiments[8] using radioactive elements such as strontium, phosphorus, and plutonium as sources of radiation within the body, it became known that relatively large doses were required to produce cancer. These doses not only were delivered over a long period of time, but were in excess of what would be used in modern radiation therapy.

Leukemia, carcinoma of the skin and bone sarcoma have been caused in some patients by injudicious exposure to x-ray and radium sources. These cancers are usually preceded by prolonged tissue changes. The current popular use of artificial radioactivity demands the protective restrictions imposed by the Atomic Energy Commission so that unfortunate sequela may be kept to a minimum in future years. It has been shown that single doses of radioactive isotopes in animals may have an effect very similar to that of repeated or prolonged dosage.

All this clinical knowledge and experimental data has prompted revisions of an estimated tolerable daily body dose which should not produce any permanent physiological changes in an average person. This "tolerance" daily amount of roentgen or gamma radiation adds up to 0.3 roentgens per week. With radioactive isotopes the tolerance dose to any body tissue or area would be 0.3 rep per week (roentgen equivalent physical).

Whether this amount should or could be exceeded repeatedly is a question that places upon the radiologist a tremendous responsibility for

the safety of the professional attendants as well as the patients.

Recent experimental work on animals has demonstrated that there are many factors which afford protection against radiation effects. A beneficial influence upon radiation effect and radiation recovery has been obtained by (1) the transplantation into a peritoneal cavity of an infantile spleen[9, 10], administration of spleen suspension[9, 10], mouse embryo suspension[9, 10], and spleen homogenate[11] (2) bone marrow injections[12] (3) large doses of streptomycin[13] (4) desoxycorticosterone injections[14], (5) massive blood transfusions[15] and (6) pre- and post-irradiation parabiosis[16, 17, 18, 19, 20].

Conclusion

The future of radiation therapy like other medical-surgical specialties will be strongly influenced by the sincerity and interests of the men and women who are today entrusted with the training programs. The radiologist should share with his scientific colleagues a greater respect for their specialities, but at the same time he should demonstrate aggressive radiological opinions when these opinions are based upon verified radiobiological evidence

Greater knowledge of the basic scientific and clinical facts, together with sound judgement, will permit the newer and improved radiological instruments and technics to fulfill the great expectations that cancer patients hold for them.

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SUNDRY CANCER RESEARCH PROBLEMS AND THEIR CLINICAL APPLICATIONS

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Obviously, this discussion can cover but a few questions in cancer research. Therefore, you must bear with me for exercising a choice which will be, necessarily, my own. The research on which I should like to report has not been done by me, but by various members of the staff of the Lankenau Hospital Research Institute and The Institute for Cancer Research in Philadelphia.

We start with the statement, as emphasized by Dr. Heller in his discussion before me, that cancers differ widely one from the other. Thus, cancer of the lower lip is quite different from cancer of the cervix or the stomach which, in turn, is different from cancer of the lung. It is possible, on the other hand, at least to pick out common denominators of cancer and set up questions in this wise. Depending upon the point of view, some investigations concern similarities and others dissimilarities. In the present case I shall try to pick out a few similarities.

One of the things which no cancer cell does is to differentiate as do normal ones. This is not to state that the differentiation of the cells in certain cancers is not quite high—which is another way of saying that they differentiate to the point of real specialization; but always from their anatomy it can be seen that their differentiation has something abnormal about it. Actually, this is the basis for the smear technic used in the diagnosis of cancer. In fact, the cells of certain cancers differentiate to the point of developing inside of themselves tiny laboratories which fulfill highly specialized functions. Thus, certain thyroid cancer cells pick up iodine, and if we offer them radioactive iodine they absorb it and thus reveal the presence of radioactivity, as determined with the Geiger counter.

Carrying this thought one step further—differentiation in certain hormone-producing tumors sometimes reaches the stage where a diagnosis can be made over the telephone. If you are told that a five-year-old girl has developed pubic and axillary hair, that her breasts have grown, that she bleeds from the uterus, and likes the boys more than is ordinary for a five-year-old girl, you may, with a good chance of success, diagnose a granulosa cell tumor of one or both of her ovaries. This, again, is part of the differentiation problem.

Even though cancer cells do differentiate, they never organize in the sense that they grow harmoniously with other cells in the neighborhood and produce organs and parts. If they did, an individual developing cancer of the tongue would develop another tongue instead of the cells growing every which-way,—a phenomenon which someone has told me would be good for double talk! But cancer cells do not "organize," if we use this word in the above sense.

Here are, then, at least two common denominators, (1) differentiation, and (2) organization.

As in any other biological process, or for that matter in any scientific investigation, it is essential that we compare our experimental material with proper controls. In the case of the failure of normal differentiation of cancer cells we must know something of normal differentiation. Many hours could be spent if we would delve into this differentiation problem—but we have time for only a few bald statements.

In the first place, no quantitative measurements of degrees of differentiation have been evolved. The microscopist says that a cell is undifferentiated, or partly or completely differentiated—which are but qualitative terms. This is unfortunate, but such is the case.

Another point, and an important one too, is that an undifferentiated cell has a choice of several paths which it can traverse. In this

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respect it might be compared with a human being, who may become a shoemaker, dentist, lawyer or farmer, depending on his personal choice and the accident of his sociological environment. It is just so with cells; when their own potential and the field influences of their immediate environment have directed their path of differentiation—to a skin cell, muscle cell or whatever—and have proceeded well on their way, there is no turning back. A most important time in the life of a cell is when this choice is made; it is called the "time of determination." Differing from human beings who can tell us that they are going to be a shoemaker, plumber, or whatever, the cell does not tell us when it has determined what it shall do. Nor can we find out by looking at the cell. We must have patience and see what choice the cell has made by watching what happens. Therefore, when we talk about pre-cancerous lesions, intradermal cancers, etc., we are putting ourselves in the position of being prophets, without real evidence on which to base our prophecies. If the biologists cannot tell from material which they may observe under the microscope while it is living and actively exerting its functions, how can we, as pathologists, by merely looking at a small piece of tissue, fixed and stained, tell what would have happened had the piece of tissue not been removed when it was?

To compensate for this lack of ability, we use the statistical method. Knowing that cancers will develop in a certain number of distorted areas of a few individuals, and knowing also that we can't tell which of these individuals will be the victims of invasive growth, we recommend that all such distortions be removed, so that none will develop into cancers,—another differentiation problem!

Now to come to specific experiments in cancer research:

Drs. Briggs and King in our laboratories asked the question: "What are the relative roles of the nucleus and cytoplasm in the differentiation of a cell?"

The most highly organized differentiation system is, of course, the fertilized egg, and as such lends itself to many experiments. An important question being attacked in our laboratories by Drs. Briggs and King, using frog eggs, concerns the relative roles of nuclei and cytoplasm in both normal and abnormal differentiation. Experiments to pursue this problem have been done, first, by examining the potentiality of the cytoplasm alone. This was done by removing the nucleus of a frog egg and then stimulating it parthenogenetically to divide. Such eggs went through several cell divisions, producing a mass of several thousand non-nucleated cells in about 24 hours. Cell division then stopped and none of the "anucleated" cells differentiated. Therefore, without a nucleus the cytoplasm is capable of only limited cell division and has no ability to differentiate.

The next question is: "What happens when the nucleus of another cell is transplanted into an enucleated egg?" This delicate operation required much practice, but is now being done very successfully. When the transplanted nucleus comes from an apparently undifferentiated cell as, for example, one of the cells of a blastula, the egg receiving it starts to divide and eventually forms a whole new normal animal. This shows that nuclei of early embryonic cells are really undifferentiated, i.e. are still equivalent to the nucleus at the beginning of development.

The next problem was to see if this is true of nuclei of cells further along in embryonal life and, hence, in differentiation. Are these nuclei still undifferentiated and capable of participating in all kinds of differentiation when put back into enucleated eggs? Nuclei from nerve cells or presumptive nerve cell or gut cells were treated in this fashion. Are such nuclei now irreversibly changed so that in combination with undifferentiated egg cytoplasm they limit the development to a cell type like that of the cell from which the nucleus was taken? This problem is now being tested, and nuclei further and further along in development are transferred into enucleated

eggs. In later stages it has been found that the eggs divide but fail to differentiate normally. This indicates that gut cell nuclei, for example, may in fact be differentiated—but more remains to be done to clearly specify the nature of the nuclear change.

These experiments, with the delicate technic which Briggs and King have developed, are definitely establishing controls for the next steps in the work—namely, the transplantation of nuclei of cancer cells.

As another type of experiment I choose to tell you of the work done by Dr. Hauschka and his associates in our Institute, on the question of chromosomes in tumor cells.

Cancer is a very variable phenomenon. Here is a patient with a huge primary tumor and practically no secondary growth. In the next bed is another patient with a small primary tumor and many metastases scattered throughout the body. Here is another with huge deposits everywhere, and yet not cachectic. Still another patient with a small cancer is cachectic to a marked degree. What are the mechanisms underlying such differences? Let us take first the question of why some patients develop many metastases from a small primary tumor, and why others develop practically no metastases from a large primary growth. Is there anything in the peculiarity of the cells of the different cancers, or is it in the host, or in both?

Dr. Hauschka attacked this problem by using the ascites tumors of mice as his material. He maintains numerous strains of tumors growing as free cell suspensions in the peritoneal cavities of mice. Some grow rapidly, some slowly; some kill in a week or two, others not for many weeks. Furthermore, if they are transplanted from one mouse to another, at times they will "take" and at other times not. By counting the chromosomes in these tumor cells, which provide admirable material for such studies, he and Dr. Levan have found, first, that there is much variation in the individual cells, and that many ascites tumors are composed of mixtures of large and small cells with sizes in between. It has been possible for Hauschka to pick out one cell from such a heterogeneous group and transplant it into another mouse, whereupon the cells derived from the transplanted single cell are much more uniform than the original tumor. This makes it easier to count and correlate chromosome numbers. In brief, he has found that very seldom do ascites tumor cells have 40 chromosomes within them, which is the number for normal mouse cells, but usually a few or many more. Most cells of some tumors actually have almost double the normal number, i.e. about 80, but seldom exactly 80. Still others have around 45. The crux of the findings is this: when the number of chromosomes in mouse ascites cells is balanced at 40, they are transplantable only into the strains from which they arose. When the average number deviates much from 40, they can be transplanted into foreign strains. This genetic imbalance appears to change the susceptibility of the malignant cells, not only to antibody, but to chemotherapeutic agents and radiation as well. Many questions have been crystallized from these findings and others, which Dr. Hauschka has published, but which cannot be rehearsed here.

Naturally, if there are twice as many chromosomes as normal, each cell receives a much larger gene dosage with which to work. Is it possible that such cells can lose some of their chromosomes without feeling it? Does it interfere with their viability? Do the different metastases of human tumors have different numbers of chromosomes within their cells? Is there a variability which helps determine the spread of metastases, rates of growth, susceptibility to irradiation and to some of the chemotherapeutic agents now under trial? What about the qualitative differences between the chromosomes when doubled, or tripled, or quadrupled? What influences have these in addition to the quantitative effect?

Work on human chromosomes is much more difficult, but it must be done. Among others, Pomerat and Hsu in Texas are obtaining information on this point.

Finally, I might emphasize that the questions propounded are of importance in our thinking along chemotherapeutic lines and in planning substances for trial. Everyone who has used some of the chemotherapeutic substances such as the nitrogen mustards, the anti-folics, and others, has observed regression in tumors. In other cases no improvement at all occurs, in still other cases (and perhaps these are the most interesting), of a number of metastases a few will respond and others continue unhindered on their way. What part do chromosome numbers and their quality play in such phenomena?

For instance, it is a fact that Law, astounding though it is, has strains of mouse leukemia cells which are quite susceptible to aminopterin; others pay no attention to it; still others require it for their growth and survival. Shall we boldly say, even though the geneticists will object quite strenuously, that "mutations" occur in cancer cells, or shall we think in these terms—that aminopterin, for instance, in a human leukemia case has dissipated a large number of leukemic cells, ofttimes to the point where it is impossible to find them in a blood smear, only to have the leukemia return; that the aminopterin has picked out the sensitive cells and allowed the resistant cells to continue living until finally they caught up and the leukemia is back again in its clinical form? Does the same thing happen in irradiation sensitivity and resistance? Is there a change in internal mechanism of the cells or is there a selection? The bulk of the evidence at present is for selection, but the other possibility is by no means excluded.

In this brief presentation, then, I have tried to pick out but two pathways along which cancer research is traversing. As in all good research, as you will have noticed, more questions are posed than are answered by the research itself, but this is the way progress is made—and progress in cancer research, while seemingly microscopic, is nevertheless steady, and we know much more about mechanisms than we did but a few years ago.

Lankenau Hospital Research Institute and
The Institute for Cancer Research
Philadelphia 11, Pa.

DR. HELLER: Thank you, Dr. Reimann.

Ladies and gentlemen, you heard the presentation, you have seen the enthusiasm of the essayists. I realize that this is the bewitching hour, but if Dr. Cornbrooks would allow us, we might have time for just one impelling question or so. *If* you have a question you would like to direct to one of the participants, I am sure they will be pleased to answer it. Has anyone a question? (None)

Well, it would appear, Dr. Cornbrooks, that the essayists have covered the subject very completely and adequately. On behalf of the Panel, I thank you, very much.

I will now turn the program back to Dr. Cornbrooks.

NEW CONCEPTS IN THE PATHOGENESIS AND TREATMENT OF CORONARY ARTERY DISEASE[1]

SIDNEY SCHERLIS, M.D.[2]

The subject about which we are speaking this morning is a very old one. In 1768, Heberden wrote a paper entitled "Some Account of A Disorder of the Breast." He described angina pectoris, but he did not know it was due to heart disease. He described a painful sensation of the breast complained about by patients after walking and especially after meals, later being found at rest, and he observed that it occurred primarily in men, almost all over fifty, "most of them with a short neck and inclined to be fat." He proceeded to say that "What the particular mischief is which is referred to these different parts of the sternum, it is not easy to guess. It may be a strong cramp or an ulcer or possibly both. It is most probable that a strong spasm be the cause of the disorder." Concerning treatment, he confessed that he knew one patient who set himself a task of sawing wood a half hour every day and with this procedure was practically cured of his disease.

We have come a long way since then but most of us do not knowingly prescribe sawing wood for one-half hour as a treatment for the disease. The disease is more frequent, it is more commonly diagnosed.

In 1950, 745 thousand Americans died of cardiovascular disease; this represents over half of all deaths in the United States during that year. Coronary artery disease is the most important cause of death from heart disease today. Much progress has been made in diagnosis, a great deal of progress in treatment, and the outlook is much better; but we still have no clear understanding of the cause and no generally accepted method of prevention.

In discussing the newer concepts of pathogenesis and treatment, I intend to select those topics which are of the most interest and perhaps show the greatest promise, and which have occupied more of the attention of observers during recent years. It has been observed that the incidence of coronary artery disease increases with advancing age.

At autopsy over 95 per cent of patients who died with myocardial infarction or coronary occlusion have atherosclerosis associated with this condition. It has been thought therefore, that atherosclerosis is the cause of coronary artery disease and that since it increases with age, atherosclerosis is an inevitable accompaniment of the aging process.

The atherosclerotic lesions themselves contain fatty material high in cholesterol. They are located at certain points in the cardiovascular system, being found where the coronary arteries angulate sharply, and in the aorta where the intercostal vessels take origin. It has been thought that perhaps trauma to the vessel plays a part in the localization of atherosclerosis. It has been suggested that the reason atherosclerosis is more common in hypertension is because associated with hypertension there may be some instability of the lipids in the bloodstream, and that they are perhaps more likely to be deposited at the points of greatest trauma in the cardiovascular system.

Interest more recently has shifted to the metabolism of cholesterol, where it comes from, how it is deposited in the blood vessels and why. It has been known for some years that certain human diseases are associated with a much higher incidence of atherosclerosis than is present in the general population. This group includes

[1] Presented at the One Hundred and Fifty-seventh Annual Meeting of the Medical and Chirurgical Faculty of the State of Maryland on Friday, April 22, 1955, in Osler Hall, 1211 Cathedral Street, Baltimore 1, Md.

[2] Assistant Professor of Medicine, University of Maryland School of Medicine.

diabetes, nephrosis, myxedema, hyperthyroidism and certain xanthomatoses. In these conditions there is increased atherosclerosis and there is an increased level of cholesterol in the blood. Because of the association, studies were done on animals as far back as 1910, and it was found that by feeding rabbits cholesterol, atherosclerotic lesions could be produced. These lesions were not similar to human atherosclerosis in their localization in that they weren't primarily localized in the brain, the heart and the kidney but they were atherosclerotic lesions.

In the chicken, feeding cholesterol would cause atherosclerosis regularly. In dogs, however, one could not produce atherosclerosis with a high cholesterol diet unless the dog concomitantly was rendered hypothyroid. So here was another clue as to what might be the underlying process and since these things could be produced experimentally, the idea grew that perhaps atherosclerosis was not inevitable. Perhaps atherosclerosis, although it accompanies the aging process, is due to specific disorders of the metabolism of the individual. Just as the diabetic cannot tolerate carbohydrates normally, so perhaps other people cannot handle cholesterol in their diets.

It was found, when the populations of the occupied countries of World War II were studied, that atherosclerosis and coronary artery disease were much more frequent among the groups of the population who could manage to obtain fat, while those who were not able to get such foods were more fortunate in that they did not have as high an incidence of atherosclerosis. Perhaps diets high in fats plus individuals susceptible because of metabolic disorder, together, add up to atherosclerosis.

There are other interesting and perchance significant observations. Atherosclerosis is much more common in the male than it is in the female, especially than in the premenopausal female. Is this due to the hormones associated with the female sex as opposed to the male, or is this due to the fact that the male has generally a much more demanding type of life than does the female? Is it tension, occupation and overwork or is it due to basic sexual differences? In this connection, while the chick regularly could be rendered atherosclerotic by cholesterol feedings, if cockerels were taken and given estrogen, in addition to cholesterol, atherosclerosis was not produced as regularly, and in some cases the atherosclerosis seemed to be reversed. The idea has gained foothold that atherosclerosis is not only not inevitable, but may even be reversible.

It has been noted that in the human female ovariectomy renders her more liable to have atherosclerosis. Some people state that eunuchs do not develop atherosclerosis as do other males; but as a gentleman commented, "This may be the cure; but I would rather not take it." There are now attempts to determine if there are certain portions of the female sex hormones which have the effect of inhibiting or reversing the atherosclerotic process but do not have the feminizing influence. Some progress is being made along these lines, and there is a good deal of promise in this field.

Cholesterol-like materials are being studied, which may "confuse" the body metabolism, in that they will be absorbed instead of ordinary cholesterol and will not produce atherosclerosis.

It has been observed, with the development of the ultra centrifuge and the determination of the different substances in the blood plasma by this method, that the male has a different composition of serum lipids, than does the female, and that this proportion of various serum lipids changes during the life of the male. It has been found that the older male has a very high percentage of certain lipids which have a large size and are comparatively light in weight and perhaps determination of the serum lipid patterns may give us a clue as to which persons are unable to handle cholesterol, and which persons might be more likely to develop atherosclerosis.

In the light of these studies, people have been wondering whether low cholesterol diets are advantageous. Is rigid restriction of cholesterol

justified, and will such diets tend to reduce the incidence of these lesions? There is no categorical answer to that question. Most people feel that a diet which is generally low in fats and not specifically in cholesterol may be advantageous, especially for those who may not be able to handle fats. A person on a low cholesterol diet will manufacture cholesterol from other substances and so have cholesterol in his blood.

Recent reports suggest that saturated fats are more likely to cause atherosclerosis than are unsaturated dietary fats.

The administration of so-called lipotropic substances such as choline, methionine and Vitamin E, actually do not effect the development of atherosclerotic lesions. It has been shown also that estrogen can convert the male pattern of serum lipids to one more closely resembling a female pattern, again emphasizing the promise that is held in this particular approach to the problem. It has been observed that heparin in fatty serum tends to clear the serum. In cholesterol-fed rabbits, heparin retards the development of atherosclerosis.

So far I have been talking about studies based upon demonstrations of cholesterol in the atherosclerotic plaques of the coronary vessels, and the emphasis has been therefore upon anatomical findings; but there are other important aspects of this matter which deserve consideration. Some years ago, it was observed at the Massachusetts General Hospital that myocardial infarction occurred in only sixty per cent of 267 patients who had coronary occlusion; and that of 261 patients with coronary thrombosis, only fifty per cent developed myocardial infarction. Therefore one may have infarction without coronary occlusion and coronary occlusion without infarction.

Therefore, we need not conclude that everyone who has atherosclerosis need develop coronary thrombosis, and also that everyone who has coronary thrombosis need not develop resulting myocardial infarction. Why does it happen in some and not in others? Atherosclerosis is a gradual process; presumably coronary thrombosis in its clinical manifestation is an acute process. What converts the gradual atherosclerotic process of sixty years to the acute myocardial infarction we see the next day?

We know that people with angina pectoris may have angina not only with exertion but with certain types of emotional stress. There are people who can walk five or six blocks with no discomfort at all but who, upon discovering there is someone at the other end of the telephone line who is unpleasant, may experience sudden anginal discomfort. There are people who can walk five blocks in warm weather without discomfort who, upon walking fifty yards in the cold wind experience angina. There are patients who can walk five or six blocks before a meal, who upon attempting to walk a shorter distance after a meal will experience angina pectoris. Perhaps they need only overeat to experience angina pectoris. An acute episode of gallbladder colic can result in coronary insufficiency, and in some cases more severe results have developed.

There are people who can have angina for five or six days with certain types of stress and for the next few weeks have no angina at all with stress which far exceeds that which previously caused symptoms. There is a variability in the precipitation of symptoms associated with emotions, with cold, with foods and certain organic disturbances. Again, in well documented cases from thirty to seventy per cent of patients who present themselves with acute myocardial infarction have premonitory symptoms. They may have had severe pains for a day or angina for a week or for a month or so. But they so frequently have had symptoms for some time before the obvious severe episode that, looking backward, one wonders—if only a physician had seen this patient when he first had his discomfort, perhaps he could have prevented further trouble. When we do see these people we should say, "This means something acute is happening to the coronary circulation." Even if we then take a cardiogram and perhaps find it entirely normal we should put the person to bed.

Some of these people within a week may develop obvious electrocardiographic evidence of myocardial infarction and we compliment ourselves upon having put the patients to bed so quickly. But there are others who are kept in bed for one week or so in whom no electrocardiographic changes appear, and who then resume activity with no symptoms or with occasional angina. Have we prevented more serious trouble in the latter by putting them to bed early, or in those with no residual angina was it some noncoronary disease in the first place?

In those with chest pain who are put to bed promptly with a normal electrocardiogram, and who develop obvious evidence of myocardial infarction one week later, what was it that was present the first day? If they had coronary thrombosis the first day, perhaps they should have had electrocardiographic changes and other evidence of myocardial damage then, because in the experimental animal who has good collaterals and who does not have atherosclerosis, tying off the coronary artery produces practically immediate changes in the electrocardiogram, and changes are not delayed for a week. Could the initial symptoms in these patients be due to something else? Could they be due to "spasm" and perhaps could coronary thrombosis in the susceptible person be a resultant of factors in addition to coronary atherosclerosis?

In connection with this, we know neurogenic stimuli can effect the coronary circulation and perhaps such stimuli, perhaps the "spasm" that Dr. Heberden spoke of in 1768, really does exist. We act as though it does, because clinically we give nitroglycerin, which we believe dilates coronary vessels.

Is there an additional mechanism for the localization and precipitation of the myocardial infarction? In other words, we all have atherosclerosis as we get older in greater or lesser degree, depending perhaps upon diet, sex, hypertension and things of that sort. Perhaps the forerunner of the coronary occlusion and resulting infarction in some persons is a sclerotic coronary vessel with super added spasm. Perhaps under certain circumstances the spasm narrows the bloodstream, slows the rate of blood flow, renders the blood more easily clotted and tends to predispose to the formation of a thrombus at this site. At least we know that in many persons overworry seems much more important than overwork in the precipitation of angina and perhaps in the background of coronary occlusion.

What about the treatment of this disease? The obvious thing to do would be to say, "Let us prevent it and you wouldn't have to worry about it." Can we prevent it? We have just discussed the factors which diet may play, and we believe that a diet comparatively low in calories, and generally low in fat (not necessarily low in cholesterol per se) may be beneficial. Perhaps in the future there will be substances that will displace cholesterol in our diet.

I think the avoidance of tensions is important as a precipitating factor, especially the older one gets. In the recurrence of coronary occlusion in patients who have had previous episodes, tension seems to have played a great role. Proper care for severe gastrointestinal disturbances and gallbladder disease is very important, as these may well be contributing and precipitating factors.

Early diagnosis doesn't prevent the disease but it may prevent some of the complications thereof, and in this regard one must realize that *angina is not a diagnosis but is a symptom.* Angina may be the result of a previous myocardial infarction and a patient may have angina for many years. *But* angina of recent onset means that something recently has happened to the coronary circulation, and a person with recent onset of angina must be treated as though he has had a recent acute coronary episode of some sort.

As for treatment, once a patient has the clinical manifestations of the disease, what do we do? First, I shall discuss the aspects of medical treatment which might be controversial. Rest, of course, is essential, because since the heart has to keep on beating, and the coronary circu-

lation is inadequate, the less work the heart has to do the better. Rest in bed or chair? I think the chair is perfectly safe *after* the person has been in bed for about four weeks.

We all know that if there has been coronary occlusion, and if myocardial infarction develops, the myocardium is weakest after about ten days or two weeks. That is not the time to get the patient out of the bed, in my opinion. Bed rest may be oldfashioned but is justified for a period of several weeks at least.

Mental and physical rest, of course, are important and sedation is in place.

Anticoagulants are not only stylish but they have been well documented as being useful. They should be used only with careful laboratory control. In large series, mortality with anticoagulants runs about fourteen per cent for the acute episode. Without anticoagulants, it runs about twenty-four per cent in controlled groups, so that anticoagulants for the acute stage are certainly justified, probably in all cases of myocardial infarction where laboratory control is available. For the chronic stage, we do not have comparable sets of figures and no statement can be made as to the efficacy of the long-term anticoagulant treatment.

We can give certain drugs which we hope dilate the coronary vessels. Experimental work is so difficult to interpret in this field and psychic effects are so important that every physician has his favorite coronary vasodilators. My own preference is for paveril.

In some cases of angina anything given with confidence will help. There are patients with angina who are helped by being given a pill which has no pharmacological effect; but the psychic effects of the manner in which it is given is very great. This emphasizes the importance of treating the patient with confidence.

I think there is one drug that is very important in the treatment of the acute coronary and that is atropine, because atropine seems to inhibit certain vasoreflexes which may tend to constrict the coronary vessels. At least the people who die on the bedpan, while being treated for coronary occlusion have had a strong vagal influence straining at the bedpan. People who have angina following meals and not before are frequently prevented from having such symptoms by taking atropine before meals. The use of atropine under these circumstances is, in the eyes of many, necessary.

It is important that we treat the patient's symptomatically. We shall not here discuss the treatment of complicating heart failure with digitalis, anoxia with oxygen, etc., because they do not involve new concepts, and are no longer controversial.

Treatment presents a greater problem in the chronic stage. For the person who has no symptoms the problem is greatest. We treat the patient who may have heart failure after he has gotten over his acute occlusion with digitalis, diuretics, salt restriction, etc. For the person who has angina and finds it necessary to take nitroglycerin to relieve the discomfort when it occurs, it is more important to prevent the discomfort, not because it may be so severe; but because each time he experiences anginal discomfort it means at that moment the coronary circulation is inadequate, at that moment the myocardium is suffering from ischemia. There are now long-acting nitroglycerin preparations which seem to prevent angina in people who otherwise experience it. In patients whose angina is related to meals and to cold, atropine before the meals seems to be of benefit.

What about the person who has no angina and no failure? Does he need any treatment? We advise him against undue stress and strain, both mental and physical. In people who have once had a coronary thrombosis we know the background for the precipitation of another attack is psychic as well as physical in many instances. Although there is no evidence overwork damages the normal heart, we prefer that he avoid strenuous exertion, but may engage in moderate activity. Most of those people are better off working than they are not working,

and should be encouraged to resume their occupations if consistent with the principles outlined.

Need we do anything else? Statistics show that in the acute stage fourteen to twenty-five per cent will succumb, depending on the use of anticoagulants, severity of the disease, etc. What about the other seventy-five per cent who recover? In the best series which I can obtain figures for, no more than about sixty per cent survive ten years following the acute myocardial infarction. In many groups of patients survival rate is much less.

The outlook is much better than it has been, perhaps because treatment is better; perhaps also because diagnosis is earlier, so we are including more mild cases in our series nowadays, but the fact remains that most people who have coronary occlusion and myocardial infarction eventually will die of that disease.

Can anything be done to prevent that high expectancy of death rate from a disease we know exists in these patients? Attempts have been made to do so as far back as 1935, an attempt was made to improve the coronary circulation by taking the pectoral muscle and suturing it to the myocardium. A little later on another attempt was made by taking the omentum up through a hole in the diaphragm and suturing it to the myocardium. Both of these methods seemed to improve the circulation through the myocardium. Lung has been tacked on to the denuded heart in an attempt to improve the circulation. There are other procedures which are more simple to perform. Talc or asbestos has been placed in the pericardial sac, and this will produce a sterile pericarditis and definitely increase the circulation to the myocardium. This is not a new procedure. It is widely done in many places, and physicians are no longer timid about so advising in properly selected cases.

Some of the newer procedures involve taking blood vessels and either anastomosing them to the coronary sinus, thereby improving circulation or by actually imbedding a vessel, such as the internal mammary artery, directly into the myocardium. At University Hospital we are interested in removing possible vasoconstrictor influences on the coronary circulation by cutting certain nerves going to the heart. This and some of the other procedures described, have yielded promising results in carefully selected patients.

With the lessening of the risk in certain operative procedures and with the growing awareness of the importance of the problem and of the future which lies ahead for many of these patients, we hope there will be a wider application of measures designed to improve the coronary circulation directly. We must not ignore the fact that coronary circulation is dependent not only upon the large vessel in the myocardium, but depends upon the smaller vessel, and the smaller vessels perhaps can be dilated by certain drugs and perhaps can be dilated by measures which may inhibit the normal tone which may exist.

Surveying the field of coronary artery disease, from the long-term point of view, interest has for a long time centered upon the atherosclerotic lesion. Work now is being done about preventing the formation of that lesion, perhaps in reversing such lesions. Dynamic factors in the pathogenesis of coronary thrombosis deserve further study. A great deal has been accomplished in treating people during the acute phase of their disease. More work lies ahead in preventing recurrences of episodes in patients who have formerly had attacks, and in compensation for the ravages wrought by the disturbance in their coronary circulation.

1214 North Calvert Street
Baltimore 2, Md.

Component Medical Societies

ALLEGANY-GARRETT COUNTY MEDICAL SOCIETY

LESLIE E. DAUGHERTY, M.D.
Journal Representative

PHYSICIANS' SECRETARIES ATTEND LUNCHEON

Excerpts from introductory remarks made to the assembled secretaries to Physicians of Allegany County, in the ballroom of the Fort Cumberland Hotel, Cumberland, Maryland, on November 28, 1956.

"Greetings, from the Allegany-Garrett County Medical Society! To my knowledge, this is the first time the Physicians' secretaries of Allegany County have ever assembled together for any purpose. This could well be a Chapter of the National Association of Physicians' Secretaries; namely, the Allegany County Physicians' Secretaries Association. This month there was founded a National Association of Physicians' Secretaries, in Portland, Oregon, at the semiannual meeting of the American Medical Association. Some notable purposes were proposed and nothing but good can come out of such an organization. Were it possible, I would like to address you as a Chapter of Western Maryland.

"In 1799, a hundred and fifty-seven years ago, three of our local physicians, headed by Dr. George Lynn of Cumberland, rode horseback along with ninety-eight other physicians from Baltimore and the several counties, to Annapolis, to partition the General Assembly then in session, for a charter to establish the Medical and Chirurgical Faculty of the State of Maryland.

"In 1868, eighty-eight years ago, the first assembly of Physicians of Allegany County gathered together, for the purpose of forming a Medical Society; in the office of Dr. Charles H. Ohr, at the corner of George and Union Streets. To this group, Dr. Ohr was elected the first president and between this hotel and his office, a full city block, was Dr. Ohr's cow pasture. Many Cumberland citizens drank raw milk from the Doctor's cows; and one of Cumberland's beloved Physicians, Dr. Charlotte B. Gardner, carried milk to her home as a child. Dr. Gardner now resides on Columbia Street, in semi-retirement.

"Disease and sickness was really a problem in those days, before pasturization of milk, smallpox vaccination, diptheria antitoxin and penicillin. Typhoid fever, about which you almost never hear, was rampant and upwards of hundreds of cases were present at all times, in Western Maryland.

"Today, we have one of the finest health records in the nation and one of the lowest death rates. We have assumed the obligation to cure and prevent disease and to this end, we have and are doing well to provide medical care in the hospitals and clinics of our city. To provide care in the home, where we realize more and more that people must be cared for in the future and because there is a limit to which we can provide adequate hospitalization in the minor illnesses, we must give thought not only to the medical care, but to the economical medical care, which the people can afford and most of all, to protect people economically, in providing Health and Sickness Insurances for those catastrophic occurrences which fall in every family now calculated with actuarial accuracy.

"Insurance Companies have done well, to provide for these necessities to those who could afford it. To that great mass of people who could not afford the necessarily higher rate, the Physician directed his thoughts to the cooperative effort of the Medical Profession and Civic and Professional groups, to provide medical insurance at a price he could pay not only for himself, but his entire family. The culmination of this cooperative effort, was the establishment of the Blue Cross Hospital Insurance Plan, in 1937 and later, the Blue Shield, in 1950. This is the Physician's own Plan throughout the nation and now enrolled are forty million people in Blue Cross and twenty million in Blue Shield. Your Physicians agreed to underwrite it with their cooperative participation. Today, it is the greatest Medical Care Program in existence.

"With this background, I want to present Mr. Charles A. Rittler, who is Field Representative of the Medical Care Program, in Maryland, Blue Cross and Blue Shield, who will speak to you of some things that will promote a better understanding of the Blue Shield Plan."

Mr. Rittler discussed Blue Shield to approxi-

mately fifty secretaries of Physicians throughout Allegany County. The consensus of opinion was, that the secretaries now have a better concept of what Blue Shield covers and the best methods of preparing the necessary forms.

PERSONALS

Dr. H. W. Eliason, Cumberland, Md. gave an illustrated talk to the local Rotary Club, on Public Health matters, dwelling on the Salk Polio Vaccine in particular, in December.

Dr. Samuel M. Jacobson, was feature writer on the Saturday church page of the Cumberland Times-News. His subject was, "What Religion Means To Me." Dr. Jacobson was one of three writers, to write on the same subject appearing weekly through December. Also writing were, a Protestant and a Catholic.

Dr. Earl R. Paul, has opened an office in Cumberland, for the general practice of Surgery.

IN MEMORIAM

Dr. William E. Moseley, 73, of Mt. Savage, Maryland, died on November 21, 1956, of generalized arteriosclerosis.

ANNE ARUNDEL COUNTY MEDICAL SOCIETY

STUART M. CHRISTHILF, JR., M.D.
Journal Representative

Dr. Donald H. Hooker, former Annapolitan, and present Acting Chief of Thoracic Surgery at the Veterans Hospital, Baltimore, addressed the Anne Arundel County Medical Society at its quarterly meeting held at the Garden Inn, Pasadena, Maryland on Thursday evening, December 6. Dr. Hooker's interesting address was illustrated by films and was very favorably received.

A report on the State convention by Dr. Randall McLaughlin, Anne Arundel County Delegate, was read.

Dr. Phillip Briscoe, President of the Society, discussed the matter of Dependent Care for service personnel in this area and the implications of the new public law in this regard. Dr Walter M. Weber of the Navy Dependent Service is scheduled to amplify this with more detailed information at the Staff meeting of the Anne Arundel General Hospital which is to be held Wednesday, December 12.

Dr. Jenkins Hamilton was approved as a new member of the Society.

BALTIMORE CITY MEDICAL SOCIETY

CONRAD ACTON, M.D.
Journal Representative

SPECIAL COMMITTEES for 1957

Dr. Francis J. Geraghty, the president, has appointed the following Committees for 1957:

JOINT ANESTHESIA STUDY COMMITTEE OF THE BALTIMORE CITY MEDICAL SOCIETY AND THE BALTIMORE CITY HEALTH DEPARTMENT:

Otto C. Phillips, *Chairman*, Mr. Todd Frazier, *Secretary*, Donald W. Benson, Frank J. Brady, Walter E. Dandy, Jr., William Carl Ebeling, Russell S. Fisher, Thomas D. Graff, Jacob C. Handelsman, Martin Helrich, Joseph D. B. King, Peter Safar, Theodore E. Stacy, Jr., Matthew Tayback, Sc.D., Mr. Harvey H. Weiss, Huntington Williams.

COMMITTEE TO PROVIDE MEDICAL COVERAGE FOR THE BOY SCOUT CAMP AT BROAD CREEK:

Karl F. Mech, *Chairman*, Edmund G. Beacham, Harold P. Biehl, A. S. Chalfant, Robert G. Chambers, Norman B. Cole, Ernest S. Cross, Jr., Robert W. Johnson, III, Lauriston L. Keown, Joseph D. B. King.

COMMITTEE TO ADVISE THE DIRECTOR OF THE BALTIMORE CITY CIVIL DEFENSE HEALTH SERVICE:

H. Alvan Jones, *Chairman*, William R. Bundick, George H. Brouillet, Raymond M. Curtis, William E. Gilmore, Edward L. J. Krieg, William G. Marr, Zachariah R. Morgan, S. Edwin Muller.

CONSTITUTION AND BY-LAWS:

Moses Paulson, *Chairman*, Marius P. Johnson, Lawrence R. Wharton, Sr.

COMMITTEE ON EMERGENCY MEDICAL CALLS:

Francis W. Gluck, *Chairman*, Nathanial M. Beck, Thomas J. Brennan, Philip D. Flynn, William H. Kammer, Jr., Herbert W. Lapp, John W. Machen.

COMMITTEE ON GERIATRICS:

Herman Seidel, *Chairman*, Walter A. Anderson, W. Grafton Hersperger, Louis Krause, H. Edmund Levin, J. Douglass Shepperd.

LEGISLATIVE COMMITTEE:

Charles R. Goldsborough, *Chairman*, Harry J. Connolly, Edward F. Cotter, Ralph G. Hills, William J. McClafferty.

MAGISTRATE'S COMMITTEE:

Sullins G. Sullivan, *Chairman*, Bernard J. Cohen, Manfred S. Guttmacher, Robert F. Healy, William H. Mosberg, Jr.

JOINT COMMITTEE ON MATERNAL MORTALITY:

Huntington Williams, *Chairman*, Irvin M. Cushner, *Secretary*, Margaret B. Ballard, J. Brooke Boyle, Jr., George H. Davis, Nicholson J. Eastman, John J. Erwin, Vincent de Paul Fitzpatrick, Jr., Arthur L. Haskins, D. Frank Kaltreider, Theodore Kardash, William Schuman, Matthew L. Tayback, Sc.D.

MEMBERSHIP COMMITTEE:

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Hammond J. Dugan, Jr., *Chairman*, Benjamin S. Rich, A. A. Silver, George L. Stickney.

COMMITTEE ON PUBLIC MEDICAL EDUCATION:

Harry M. Robinson, Jr., *Chairman*, Houston S. Everett, H. Hanford Hopkins, Lauriston L. Keown, Amos R. Koontz, E. Roderick Shipley, Martin L. Singewald.

The Executive Board met Tuesday, 23 October, and a very controversial subject was broached. Representatives of the two teaching hospitals discussed their plans in relation to charges to the private patients of "full time" staff members. There was, of course, much concern as to how this accorded with Maryland State Laws regarding the corporate practice of medicine and with fairness to private practitioners generally. Since the plans were stated to be in flux, it was decided to make no recommendations until a definitely illegal aspect was demonstrated.

Action "before 26 October" was asked on the proposed Fee Schedule for the Armed Forces Dependents Medical Care Act. The Board passed the schedule from hand to hand and each member reviewed it briefly. No gross discrepancies were found and it was approved, since the compensations appeared adequate. This makes the second time that an important decision concerning Federal medical practice has been presented to the Society for approval before an imminent deadline that "must" be met. Such urgency causes a plain Journal Correspondent to wonder why Federal medical planners need a rubber stamp at the local level. It is said that socialists fear public opinion most of all. This "rush" technique apparently is effective in forestalling organized opposition or local counterplanning.

A suggestion from a member of the Society that the Baltimore City Delegates to the State Medical Meetings report, through their Chairman, actions taken at the State Meetings to the City Society at the nearest regular meeting was considered. As the Delegates are now organized it was agreed that such a report was potentially desirable, if only for the record. As a full report—with background—of what went on could easily be too lengthy and impair the Scientific Meeting, it was decided that such a report should be requested for the Executive Board for screening. Selected items will be brought to the attention of the Society.

A member of the Executive Board suggested that it ought to be made mandatory that, in order to keep one's membership in the Society, attendance at one monthly meeting per year be required. No action was taken on this revolutionary concept.

* * *

The Regular Meeting was held Friday, 2 November. President Grant Ward introduced the Society's guests from the Kent County Medical Society: Dr. A. C. Dick, President and Dr. R. W. Farr, Delegate. He also introduced Dr. Howard's guest: Dr. E. R. Boland from Guy's Hospital, London, England.

President Ward then spoke of the American Medical Education Foundation and the importance of contributions to AMEF now, not only for the principal purpose of aiding medical education, but also because of matching gifts from the Ford Foundation.

The Scientific Session was devoted to a panel discussion on "Hemorrhagic Disorders." The participants were Dr. Milton S. Sacks and Dr. Carroll L. Spurling, Professor and Assistant Professor at the University of Maryland Medical School together with Dr. C. Lockard Conley and Dr. Dudley P. Jackson, Professor and Assistant Professor of Medicine at the Johns Hopkins University School of Medicine. This learned panel integrated this rapidly

developing and highly technical field of medicine in an outstanding fashion.

The Woman's Auxiliary was on hand with coffee and doughnuts to round out the evening in fine style.

* * *

At the regular Executive Board meeting on Tuesday, 27 November, a candidate for Baltimore's "Young Man of the Year" was considered in response to the Baltimore Junior Association of Commerce suggestion that one be designated from the medical profession. A December 15 deadline was in effect, and an age limit of 35 years had been established. Most members of the Board felt that it would be good if a suitable candidate could be nominated. Of those considered, none were under the age limit, one actually becoming 36 on December 15, 1956. There were many who had advanced the profession, but few who could be considered to have directly contributed to Baltimore City's advancement.

The March meeting of the Society was noted to fall on March 1, 1957. This is in conflict with other activities in which members of the Society may be expected to participate. The Board felt that March 8th would be a more suitable date, and the meeting was specifically changed in accordance with the anticipated convenience of all concerned.

There were many reports of committees brought up for discussion. In particular, one brought to the Board's attention by Dr. Koontz related to the American Medical Education Fund. Dr. Jarrett is in charge of the Hopkins University "Roll Call" this year and wants all alumni informed on a reversal of position previously announced. In a change of policy, the Ford Foundation will *not* match funds given the A.M.E.F., if earmarked for a specific institution. Only *UN*designated funds will be matched in accordance with the previously announced plan.

Dr. Koontz also pointed out an interesting aspect of the unfolding Federal Armed Forces Dependents Medical Care Program. Service physicians are specifically prohibited from advising dependents on the selection of civilian physicians. The ascribed reason for this was that in some areas osteopaths, chiropractors, naturopaths, and irregulars of various types are licensed by state law and are entitled to the title "doctor" and have the same statutory privileges as physicians. In areas where the telephone directory's "Yellow Pages" indicate professional specialities this might not constitute a drawback, but in Maryland where no such system is used, the laity could suffer. One doubts, though, that the usual Service reference channels: commanding officer, neighbors, friends, relatives and predecessors, will fail to operate for the future as they have in the past, in the close-knit Federal communities.

* * *

The President's Meeting of the Society was held Friday, December 7. Dr. C. Rodney Layton, President of the Queen Anne County Medical Society, was our guest of the month. President Grant Ward reversed the usual procedure and had the scientific session immediately follow the introduction of Dr. Layton to the membership.

Dr. Henry Doubilet, Associate Professor of Surgery, New York University College of Medicine, presented a fascinating study of pancreatitis. He first discussed the background of his interest in sphincterotomy to relieve biliary reflux into the pancreatic duct system as the prime cause of pancreatitis. From the records of his 450 cases he felt that the catastrophe of acute pancreatic necrosis was due largely to tripsinemia and potassium loss via retroperitoneal seepage. He advised that albumin or plasma counteracted the tripsin and that potassium in huge amounts was necessary to save life. Drainage of the pancreatic and bile ducts through catheters could reverse the destructive process and permit repair to occur. Sphincterotomy after remission would prevent recurrence.

These concepts were substantiated by his pictures of radiopaque material in the ducts at various stages of injury and recovery. He demonstrated increased permeability of the pancreatic ducts to support his thesis about pseudocyst formation. His cinefluorphotographic demonstration of the dye in the biliary-pancreatic system was most remarkable. The films showed a special duodenal "second stomach" functional action in response to administered fat. He compared the churning movement to a "cocktail shaker." Bile and pancreatic juices could be seen spouting into the mass as it was worked up and down, most violently. A lively interest was aroused in the audience and many questions were asked.

In the business session that followed, the various Reports of Committees were accepted as distributed. The Nominating Committee's slate was elected unanimously. New members were elected. Past President Amos Koontz spoke in behalf of the World Medical Association and its importance to practicing physicians everywhere. It serves, he stated, to further President Eisenhower's appeal that people in different countries should meet on a direct interest level and circumvent the delays and frustrations at State Department level. He told how it differs from the World Health Organization of the United Nations, which is on a high political level. He urged all to join.

Dr. Otto C. Phillips presented a carefully prepared amendment to the constitution regarding the Nominating Committee. He proposes that some members of the Nominating Committee be elected by the Society membership at a regular meeting, instead of having them all appointed by the President. It was acted on favorably and will be sent to the Constitution Committee for study and submission at our next election.

Dr. Amos Koontz then presented a gavel to the outgoing President, with appropriate thanks and commendations that were endorsed by all.

After the meeting, we joined our Woman's Auxiliary for the termination of their Hawaiian Party in the Supper Room and for what was left of their fancy luau. Their President, Mrs. Ellsworth Cook, and her Committees, put on a fine affair. We all had a fine time talking, eating, watching a hula dancer, listening to guitar music and wearing leis. This four-year kammaaina got homesick for the Islands all over again.

FREDERICK COUNTY MEDICAL SOCIETY

LOUIS R. SCHOOLMAN, M.D.

Journal Representative

The eagerly anticipated Frederick County Medical Society election night celebration was held at the Frederick Hotel November 20th. "Mine host," the genial Mike Croghan, presided over the trays of oysters, platters of ham and pots of beans. From time immemorial the 'tab' had been picked up by the society; but this year the purchase of a new projector had depleted our treasury. But the fare was so good I, for one, did not mind.

The newly elected officers were Dr. James Thomas, president; Dr. Jesse Fifer, 1st vice president; Dr. Henry Chase, 2nd vice president. Dr. A. M. Powell, Dr. John Culler, and Dr. L. R. Schoolman were re-elected to the posts of secretary, treasurer and delegate respectively.

Two new members were present. Dr. Lawrence Fruth, anestheologist at the Frederick Memorial Hospital, and Dr. Frank Damazo, general surgeon, who has just hung out his shingle.

Hospital News

The medical staff met November 5th. Doctors Worthington, Martin and Reid, surgeon, practitioner and radiologist respectively, presented a case of intussusception of a subacute appendicitis into the caecum.

At the November conference of the obstetrical department Dr. Harry Gray presented a case of repeated caesarean section.

The Clinical Pathologic Conference case was puzzling. It was one of acute endocarditis (E. coli) with perforation of the mitral valve.

USE OF RADIOIODINE (I-131)

A one-week intensive course in the Diagnostic Use of Radioiodine (I-131) will be given March 18–22, 1957, at Georgetown University Medical Center, Washington, D. C. This course, open to authorized physicians, will meet AEC qualifications for diagnostic I-131. Further information may be obtained from Dr. B. J. Duffy, Jr., Georgetown University Hospital, Washington 7, D. C.

Necrology*

Guy Steele, M. D.
1861–1956

Dr. Guy Steele died in the Cambridge-Maryland Hospital on October 12, 1956, in the institution where he had long been a member of the Medical Staff, and during 15 years of that time had served as its Chief of Staff. He was the last surviving member of the "big four" who pioneered for the establishment of a hospital in Dorchester County.

Dr. Steele, who observed his 95th birthday in June, was taken to the hospital several months before his death for treatment of a fractured hip after he had fallen in his home.

A beloved family physician of the horse and buggy era he was widely recognized in professions other than medicine. In his early years he planned a well-rounded life which led him into the realms of teaching, surgery, genealogy, and botany. He was an official of Christ Episcopal Church, and he was recognized as a gardener who planted prize-winning flowers informally. Out of a busy schedule he set aside a certain amount of time to reclaim the graves of Revolutionary soldiers buried within a radius of 25 miles of Cambridge. As a member of the Sons of the American Revolution he placed markers at many deserted spots.

Among the early ventures of Dr. Steele was a cruise with the U. S. Navy in 1891. He was fleet pay clerk of the Asiatic Station. Later he was principal of the Cambridge Seminary; and was graduated in 1897 at the School of Medicine of the University of Maryland, holding the office of vice president of his class. In succeeding years he became the health officer of Cambridge and Dorchester County, and was also draft surgeon and a member of the draft board of World War I.

Part of his life was devoted to serving as physician at the Dorchester County Jail. He was the acting surgeon of the U. S. Public Health Service, and president of the Medical and Chirurgical Faculty of Maryland in 1917. On his 83rd birthday he performed major surgery at the Cambridge-Maryland Hospital.

Dr. Steele was the son of Dr. Thomas Buchanan Steele who started to practice medicine in Dorchester County in 1867, after having served as surgeon in the U. S. Navy.

Dr. Steele was born at Hambrook, which was built by Isaac Steele, a "great uncle four times removed." His mother was Isabella Elizabeth Henry, daughter of John Campbell Henry, who was a son of John Henry, one of the governors of Maryland and a member of the Continental Congress.

When the time came for the boy, who had ridden the dusty country roads and impassable highways with his father, to equip himself with a horse and buggy, the purchase was made with a parental blessing and a prayer that the son "would serve sacrificially." There was a supervisory period of eight years; then the father retired. The son sought out every remote section in Dorchester County, driving his steed day and night and reading medical books and magazines as he travelled over sandy and marshy roads. He cultivated an interest in the classics as well as modern literature.

Dr. Steele's devotion to his mother is enshrined in the Maryland Historical Society, Baltimore, where letters he wrote her from foreign soil are considered priceless. In the form of a diary his daily messages are treasured for their descriptions of the historic period before Communism swept over the ancient nations of Japan and China.

Dr. Steele's early experience with the Navy started when he served as a pay clerk on the U. S. S. Mohican, sailing out of the Mare Island Navy Yard, California, for a cruise of the Mexican countries, and Central America.

He had the rare experience of belonging to that group of naval officers who sailed the seven seas in the period extolled for its "wooden ships and iron men." With them he set out from Gibraltar aboard the Lancaster on one of the last cruises of the U. S. Navy before conversion to metal ships. Since the breeze was not sufficient to bring the ship across the Atlantic, it just rolled along leisurely, making the crossing in 56 days. Before its arrival in New York there was considerable uneasiness about the voyagers, but there was no way of communicating with the crew because wireless and radio communications

* Memoir Committee: A. S. Chalfant, M.D., *Chairman* John F. Hogan, M.D. and Robert H. Riley, M.D.

were unknown. Lacking refrigeration the officers and crew ate eggs preserved in brine. Dr. Steele often remarked that the trip wasn't too bad, but canned goods were eaten so much that finally all kinds of meat tasted alike. Dr. Steele prized the picture of the Lancaster which he kept on the wall of his office. Compared with the leviathans plowing the seas today, it looked very frail. Dr. Steele was photographed on the deck while the ship was docked in Yokohoma in the fall of 1893. "We were full rigged to the royals" the doctor would tell friends who liked to hear him recount experiences at Maderia, Capetown, Batavia and Singapore. "The Lancaster had a displacement of 3250 tons, and I was proud to have had a part in one of the last cruises 'under sail' in the U. S. Navy."

The Steele home is in full view of Christ Church, where Dr. Steele served as a vestryman for 20 years. Through his influence the magnificent stained glass window depicting the Sermon on the Mount was given by Charles Steele, a partner in the J. Pierpont Morgan Co., in memory of his father, Isaac Nevett Steele. In the rear of the house Dr. Steele grew choice shrubs and flowers. He liked all flowers but was particularly fond of roses.

In the realm of sports the dean of Dorchester physicians followed baseball for 86 years. He started playing on sandlots when he was nine years old. When his practice kept him from active participation he followed the home team, rooting for the home boys. He was a good shot, keenly alive to the bird and ducking seasons, declaring he could "stand as much cold as a muskrat."

When the Rescue Fire Company was organized, he was a charter member. He is the last surviving one of that group which fought fires as a bucket brigade until there was sufficient funds for purchasing a hose cart which the firemen dragged over the unpaved streets of the town in their line of duty.

Dr. Steele is survived by two nephews, Oscar Trail of Easton, and Thomas S. Trail, of Baltimore. There are two stepchildren: Mrs. W. Laird Henry, Jr. and Henry Wier, children of Mrs. Sallie Robertson Wier, his second wife, who died several years ago.

Dr. Steele's first marriage was to Miss Elsie Hughes, who was one of the superintendents of the Cambridge-Maryland Hospital.

With the passing of Dr. Guy Steele, the Dorchester County Medical Society has lost its oldest and most revered member who will always be remembered in this community.

Alfred R. Maryanov, M.D.

Lloyd Rogers Meyers, M. D.

1892–1956

Dr. Lloyd Meyers died August 12, 1956, of a heart attack. For sometime he had been ailing, but worked up until the day of his death, having done several operations in the morning.

To his colleagues, he spoke of retiring, but like most of us, it was a hard decision to make; and he never got around to doing it. For several years, he spent two or three months in Florida each year, where he had a home in Fort Lauderdale and enjoyed fishing.

His practice was limited to Eye, Ear, Nose and Throat. He served on the staffs of the Sacred Heart Hospital and the Memorial Hospital, of Cumberland, Maryland.

Born in Pennsylvania, he began practice in Everett, Pennsylvania, later moving to Cumberland. He leaves a wife and one married daughter. He was affiliated with the Masonic Lodge and the Presbyterian Church.

Leslie E. Daugherty, M.D.

John Forsyth Aubrey, M. D.

1883–1956

John Forsyth Aubrey, an Army doctor who served in both World Wars, and a sanitation officer during the construction of the Panama Canal, died in Washington, D. C., on October 4, 1956, after a long illness.

Dr. Aubrey was the son of the late Judge William Aubrey of San Antonio. His grandfather, John Forsyth, was a former governor of Georgia who served as Secretary of State under Presidents Martin Van Buren and Andrew Jackson.

Dr. Aubrey was born in Lynchburg, Virginia. He attended the University of Texas and Johns Hopkins University and received his medical degree from the University of Maryland in 1921. He lived in Baltimore for 30 years and served as surgeon at the Maryland State Penitentiary.

Dr. Aubrey served as medical officer with the 29th Division during World War I and was a surgeon at the Philadelphia Signal Depot during World War II.

He was a member of the Baltimore City Medical Society and the Medical and Chirurgical Faculty of Maryland; the American Medical Association; the Military College of Surgeons; the Panama Canal Society; the Veterans of Foreign Wars and the American Legion.

He is survived by his widow, Florence Conner Aubrey of Miami, Florida; a daughter, Ann Aubrey Brown of Cambridge, Massachusetts; a sister, Eugenia Buckley of San Antonio; and one grandchild.

Funeral services were held at the Fort Myer Chapel and burial was in the Arlington National Cemetery.

J. F. H.

Kyle W. Golley, M. D.
1898–1956

Dr. Kyle W. Golley died suddenly on September 6, 1956, in Baltimore. He was born in Templeville, Maryland, on January 11, 1898, the son of a physician.

His early education was completed in Baltimore schools and he was graduated from the University of Maryland in 1921. The following three years were spent as a house officer at Mercy Hospital where he served as chief resident during the last year. Upon completion of his resident year, he became engaged in private practice and continued to work in a most dedicated manner until the day of his death.

Dr. Golley is survived by his wife, the former Miss Rita Bockmier, whom he married in 1924; a son, James E. Golley; two daughters, Mrs. James Minor and Miss Helen Golley; and eight grandchildren.

If it could be said he had any real interest aside from his practice, we might mention his great love for music which he never lost. He himself derived much pleasure from playing the clarinet.

He was a member of the American Medical Association and the Baltimore City Medical Society.

Dr. Golley's father died at the early age of thirty-one and his death was attributed to overwork. The same can be said about his son, for he gave all his time to his patients, rarely leaving his office except for his medical duties. His loyalty, his skill, his sympathy, his humor and understanding won for him not only the admiration of his patients but also their respect and love.

D. J. Pessagno, M.D.

Paul Elliott Carliner, M. D.
1910–1956

The sudden death of Dr. Paul E. Carliner at the height of his vital and productive career was a shock and a grievous loss to his many friends and colleagues, as well as to his devoted family and the community which he served. His strength of character, enhanced by an unusually warm personality, drove him to give of himself unstintingly to many communal and humane causes as well as to his professional duties.

Dr. Carliner was born and educated in Baltimore. He was graduated from the University of Maryland School of Pharmacy in 1929, and the University of Maryland Medical School in 1934, then served as a House Officer at the Sinai Hospital under the late Dr. Charles R. Austrian, and subsequently entered upon the private practice of internal medicine in Baltimore. This was interrupted by his early request for Army duty in World War II, and he served with distinction as a captain in the 80th Division which is so memorable for the part it played in the Battle of the Bulge.

After the war Dr. Carliner returned to his practice, and to work in his field of special interest, in the Allergy Clinic of the Johns Hopkins Hospital and University. It was during this period that Dr. Carliner and Dr. Gay developed the use of Dramamine for the relief of motion sickness, and carried out their experiments with the collaboration of the U. S. Army Medical Department.

Dr. Carliner was currently engaged in the development of a suppository for the rectal administration of fixed doses of drugs which are now available only for hypodermic use.

To this full program were added his duties as Medical Director of the State Employment Commission, president of the Parent-Teachers Association of the Mt. Washington School, president of the Hebrew Immigrant Aid Society, and vice-president of the Beth El Congregation.

Dr. Carliner was a Fellow of the American Academy of Allergy, as well as a member of the staff of the Johns Hopkins Hospital Allergy Clinic, the Sinai Hospital, and the University Hospital.

Dr. Carliner is survived by his wife, two sons, and a daughter.

Library

"Books shall be thy companions; bookcases and shelves, thy pleasure-nooks and gardens." *ibn Tibbon*

LIBRARY CHATTER

LOUISE D. C. KING

Librarian

SCRAPBOOK

On

Testimonial Dinner for Dr. J. M. T. Finney, Jr.

(*Gift from Dr. George G. Finney*)

It is fitting our readers should know that Dr. George G. Finney has given us the scrap book containing memorabilia of the Testimonial dinner tendered his father, the late Dr. John M. T. Finney on February 17, 1912. This dinner and the Testimonial Fund raised at that time, was in deep appreciation for Dr. Finney's decision to decline the Presidency of Princeton University and to remain in Baltimore and continue his teaching and practice here.

The large tome is more than a scrap book; it contains portraits, the speeches made on that occasion, signatures of contributors and those declining and accepting the invitation. To glance through the book gives one a kaleidoscopic view of the names representing the best in medicine during the early part of the twentieth century. Some are not now among us, many attained no special fame, but each in his allotted place, has contributed to the progress of medicine and to the glory of the few whose names will go down in history.

The Fund raised at this time has provided, in the subsequent years, prominent lecturers for the Faculty and many books and periodicals which are a part of our collection and which are designated by a special bookplate designed by Max Broedel.

When reading one of our books, if you look on the inside of the front cover and see the beautiful Finney bookplate, may it convey to you not only that a fine surgeon was honored by the establishment of this Fund, but also that it was a great welling-up of gratitude to, and affection for, the man himself in his personal relations, that instigated it. It is perfectly possible for each of you to experience such love and devotion and we can think of no better way to perpetuate this feeling than by the establishment of a similar Fund, however small, to be a permanent reminder that one man has not lived in vain.

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You Are Invited

To

MEDICAL LEGAL SYMPOSIUM

Arranged by the American Medical Association

At

BENJAMIN FRANKLIN HOTEL

Philadelphia, Pennsylvania

Thursday and Friday, March 29 and 30, 1957

The registration will begin at 12:00 Noon on March 29th and the March 30th session will start at 9:30 A.M. and will be concluded by 4:30 P.M.

The audience will consist of attorneys and physicians. Some of the subjects will be "Trauma and Disease," "Medical Expert Testimony," "The Medical Witness," etc.

Attendance is limited. If you are interested, write promptly to: Mr. C. Joseph Stetler, American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

Health Departments

BALTIMORE CITY HEALTH DEPARTMENT

Obstetric Effects Of Work

In an address entitled "Social Barriers to Optimal Health" presented at the 20th Annual Meeting of the Mississippi Public Health Association in December Dr. Matthew Tayback, Director of the Baltimore City Health Department's Statistical Section has pointed out the obstetric effects of work during pregnancy. Dr. Tayback's studies on this phase of health is as follows:

"In considering the principal problems which are faced in the area of maternal and child health, prematurity is unquestionably a leading issue. There have been many and diverse investigations in connection with this problem. Biological factors such as maternal age and birth order have been shown to influence the risk of prematurity but the relationships found have not been marked. Differences in the prevalence of prematurity have been demonstrated among white mothers who were stratified by socio-economic status—but the order of the difference, 5.5 per cent in the highest economic fifth as contrasted with 7.4 per cent of the lowest economic fifth was not too exciting, nor did it lead to a useful concept in respect to minimizing prematurity. It did suggest the need to investigate the possible importance of income related variables such as diet, work during pregnancy and several others.

"In the recent literature on the subject, Stewart has found it possible to separate the factor of work during pregnancy from the variable of income. For each of three broad income groups it was found that in respect both to perinatal mortality and incidence of prematurity, mothers who were gainfully employed were at a significant and marked disadvantage as compared with housewives, i.e. mothers who stayed at home, and further, women who continued working in the last trimester of pregnancy were worse off than those who retired from employment relatively early.

"During the current era of full employment when young mothers are encouraged to remain active and keep on the job while pregnant, a social form of behavior has developed, which appears to interfere with the highest attainable levels of infant and maternal health."

Huntington Williams, M.D.

Commissioner of Health

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MEDICO-LEGAL WORKSHOP

The Department of Legal Medicine of the Medical College of Virginia, the Chief Medical Examiner's Office and the Virginia Society of Pathology and Laboratory Medicine, are sponsoring a Medico-Legal Workshop for Medical Examiners, Pathologists and other interested physicians, on Friday, March 29, 1957, from 8:00 A.M. to 4:30 P.M., in the Amphi-Theater and Baruch Auditorium of the Medical College of Virginia, Richmond, Virginia.

The Medical Examiners will have an opportunity to make investigations with special reference to general examinations of bodies, photographic techniques and the use of body fluids in medico-legal investigations. They will have a joint session with the Pathologists wherein gunshot wounds and special techniques with reference to this subject will be discussed. The Pathologists will see practical demonstrations of the medico-legal autopsy techniques to be employed in deaths involving stab wounds, gunshot wounds and motor vehicle-pedestrian injuries. Stab wounds and gunshot wounds will be inflicted and demonstrated.

The registration is $25.00 and registration is limited. For further information address inquiries to Geoffrey T. Mann, M.D., LL.B., Chairman, Department of Legal Medicine, Medical College of Virginia, Richmond, Virginia.

STATE OF MARYLAND DEPARTMENT OF HEALTH

MONTHLY COMMUNICABLE DISEASE REPORT

Case Reports Received during 4-week Period, January 4–31, 1957

	CHICKENPOX	DIPHTHERIA	GERMAN MEASLES	HEPATITIS, INFECT.	MEASLES	MENINGITIS, MENINGOCOCCUS	MUMPS	POLIOMYELITIS, PARALYTIC	POLIOMYELITIS, NON-PARALYTIC	ROCKY MT. SPOTTED FEVER	STREP. SORE THROAT INCL. SCARLET FEVER	TYPHOID FEVER	UNDULANT FEVER	WHOOPING COUGH	TUBERCULOSIS, RESPIRATORY	SYPHILIS, PRIMARY AND SECONDARY	GONORRHEA	OTHER DISEASES	DEATHS: Influenza and pneumonia
Total, 4 weeks																			
Local areas																			
Baltimore County	50	—	4	1	3	—	21	—	—	—	14	—	—	4	25	2	3	—	6
Anne Arundel	10	—	—	—	—	—	1	—	—	—	1	—	—	—	7	1	5	—	3
Howard	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	1	—	—	2
Harford	5	—	1	—	—	—	—	—	—	—	—	—	—	1	5	—	—	—	1
Carroll	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	6
Frederick	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	2
Washington	1	1	—	—	—	—	—	—	—	—	—	—	—	—	1	1	—	—	—
Allegany	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Garrett	1	—	—	—	—	1	2	—	—	—	—	—	—	—	—	—	—	—	1
Montgomery	15	—	3	3	2	1	54	—	—	—	21	—	—	1	6	—	—	e-1	2
Prince George's	12	—	1	1	4	—	33	—	—	—	10	—	—	—	5	2	1	—	6
Calvert	3	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Charles	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	1	—	—
Saint Mary's	6	—	—	—	—	—	3	—	—	—	—	—	—	—	—	1	2	—	—
Cecil	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4	—	2	—	—
Kent	1	—	—	—	1	—	5	—	—	—	2	—	—	—	—	—	—	—	—
Queen Anne's	—	—	—	—	—	—	4	—	—	—	—	—	—	1	2	—	—	—	—
Caroline	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Talbot	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	8	—	—
Dorchester	1	—	—	—	—	—	2	—	—	—	—	—	—	—	5	—	—	m-1	2
Wicomico	9	—	—	—	12	—	6	—	—	—	1	—	—	—	3	—	2	t-1	2
Worcester	1	—	—	—	1	—	—	—	—	—	—	—	—	—	1	—	—	—	2
Somerset	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—
Total Counties	115	1	9	5	23	2	131	0	0	0	49	0	0	7	68	8	24		37
Baltimore City	117	0	6	1	34	1	71	0	0	0	25	0	0	15	63	14	506		26
State																			
January 4–31 1957	232	1	15	6	57	3	202	0	0	0	74	0	0	22	131	22	530		63
Same period 1956	381	0	42	13	1689	4	260	1	0	0	98	0	0	25	143	24	578		89
5-year median	401	1	34	19	850	5	185	1		0	170	1	1	33	144	19	600		75
Cumulative totals																			
State																			
Year 1957 to date	310	1	19	6	62	4	239	0	0	0	81	0	0	23	168	26	759		78
Same period 1956	424	0	56	14	1955	5	318	1	0	0	105	0	0	26	197	28	687		122
5-year median	486	1	40	22	1000	6	221	2		0	188	1	1	43	176	24	780		92

e = encephalitis
m = meningitis, other than meningococcus.
t = tularemia

Woman's Auxiliary Medical and Chirurgical Faculty

MRS. GERALD W. LEVAN, *Auxiliary Editor*

DOCTORS' DAY

March 30th will be DOCTORS' DAY! Not only in Maryland but in most all of our states, as well as some of the United States possessions. And, NOW IS THE TIME for the members of the Woman's Auxiliary to complete plans for observance of the day.

Doctors' Day is a special day set aside to honor the members of the *medical* profession, past and present—the men and women who, by daily devotion to their duty of service to humanity, minister to our health and welfare.

The date of March 30th was not chosen at random, but commemorates one of the greatest discoveries for the alleviation of pain and suffering that our nation has produced. March 30 is that day, in 1842, when a famous Georgian, Dr. Crawford W. Long, first used ether anesthesia in surgery. And, by honoring the great discovery of Dr. Long we honor *all* members of the medical profession.

The idea of Doctors' Day was originated in Georgia by an auxiliary member, Mrs. G. B. Almond of Winder, Ga. in 1933. It was introduced to the Woman's Auxiliary to the American Medical Association in 1934 and to the Woman's Auxiliary to the Southern Medical Association in 1935. Today it is observed by almost every state auxiliary in the nation.

THE RED CARNATION has been designated as the official flower for Doctors' Day. Courage, strength, hope, comfort and cheer—these words symbolic of the red carnation also mark the qualities that set our doctors apart in a profession that calls for selfless service day and night to relieve suffering, physical and mental, and bring hope once more to the human heart.

Your appreciation can be shown by a hearty handshake, a smile, a card or even a telephone call—to let your doctor know that you really appreciate his personal sacrifices for your health and that of your family.

Your doctor's responsibilities are great . . . his road is hard . . . his hours long . . . his day's work never done. His constant fight to prevent illness and prolong life makes his burden heavy. His strength is repaid by the joy he feels as hearts beat stronger.

Doctors' Day is the time to remember that many would not be here at all—to criticize or to praise—if it were not for the medical help they have received. It is time to remember who is indebted to whom. It is the time when just one type of person is free to 'talk about' the doctor—those who owe him neither gratitude nor money, and never expect to call on him in time of need!

Publicity of Doctors' Day—In planning your publicity for the press, radio, church pulpits and bulletins, and perhaps television, be very sure to stress the point that we are honoring the *medical* doctors (the men and women of the medical profession, if you prefer). Emphasis is placed on this phase of publicity because of the fact that many persons enjoying a doctorate, earned or honorary, have included themselves in our observances of Doctors' Day.

The observance of Doctors' Day affords the auxiliary member an excellent opportunity to further good Public Relations for the medical profession. By paying tribute to our medical men and women, we can impress the laity with the value of the physician to his community. It is our privilege to remind the layman that he should pause and consider, at least on this one day of the year, how completely and unselfishly the medical profession is dedicated to his health and welfare. If we are sincere and tactful, we can do much to change the attitude of the public toward the doctors. Do not defend them, but explain for them.

It is important that our observances attain the real purpose of Doctors' Day—that of honoring our doctors. This objective, plus good Public Relations value, can be accomplished through:

1. Publicity—press, radio, television, store window displays, etc.

2. Proclamations—by the governor and mayors.
3. Contributions to medical and nursing school scholarships, charity hospitals, etc.
4. Other community services which further good public relations for the medical profession—health forums, public meetings, movie trailers in theaters, red carnations on hospital trays, etc.

The doctors should be afforded some relaxation from work and might derive much personal pleasure through:

1. Entertainment—dinner parties, dances, picnics, barbecues, etc.
2. Greetings and personal messages, and don't forget the ill or retired.
3. Red carnations to the doctors.
4. Coffee and sandwiches served to the doctors working in the hospitals on March 30th.
5. Honor all physicians who have practiced over 40 years.
6. Establish scholarships in medicine and allied fields in honor of local doctors.
7. Place some books of medical interest in hospital and public libraries, in honor of local doctors.

THE NEWS LETTER

Our first NEWS LETTER has been mailed to all the Auxiliary Members and to many potential members. This issue had a message from Dr. Warfield M. Firor, Chairman of the Council. He is also Chairman of its Executive Committee, which is our Advisory Committee. Dr. Firor extended congratulations on behalf of the Medical and Chirurgical Faculty, as well as best wishes for the success of the NEWS LETTER and the fulfillment of its purpose.

Every Component Auxiliary contributed and Mrs. Goldstein, the Editor, appreciates the support she has been given and hopes the members will continue their assistance by sending her ideas, news, etc. She also wishes to thank those who helped her with the stapling, stamping and addressing: Mrs. Whitmer B. Firor, Mrs. Raymond V. Rangle, and Mrs. Homer U. Todd.

Suggestions for an appropriate name for our NEWS LETTER may be mailed to Mrs. A. E. Goldstein, 3505 North Charles Street, Baltimore 18.

We, the Auxiliary, know that Mrs. Goldstein and her Editorial Staff; Mrs. D. D. Caples, Assistant Editor; Mrs. J. G. Ball, Mrs. J. S. Haught, Mrs. B. B. Kneisley, and Mrs. C. H. Williams, have given of their time, effort and thought to our new project—THE NEWS LETTER—and so I am taking this opportunity to express to them the Auxiliary's appreciation.

Judy Todd
President

LUAU FOR BALTIMORE CITY MEDICS AND THEIR WIVES

MRS. CONRAD ACTON

A "Luau," with ham and shrimp, instead of the usual "fish and poi," featured the second annual joint meeting of Baltimore's physicians and their wives which took place at the Medical Faculty Building on Friday evening, December 7.

At that time the Woman's Auxiliary to the Baltimore City Medical Society entertained the gentlemen in the Society at an "Evening in Hawaii." While the doctors present were in scientific session, their wives were entertained by a beautifully illustrated armchair tour of the Hawaiian Islands, with commentary by Mr. and Mrs. L. Park Street. The entire program, in an atmosphere of orchids, leis, soft lights and tropical music, was arranged by Mrs. Ross Z. Pierpont, the Program Chairman of the Woman's Auxiliary.

Following the separate programs, Mrs. E. Ellsworth Cook, Jr., President of the Auxiliary, greeted all guests at the "tropical luau" so beautifully arranged by Mrs. William Carl Ebeling, Hospitality Chairman of the Auxiliary.

Several of the honored guests who greatly enjoyed the feasting and authentic Hawaiian hula dancing which followed were Dr. Grant E. Ward, Immediate Past President of the Baltimore City Medical Society, and Mrs. Ward, who is also a member of the Executive Board of the Auxiliary; Dr. Frank S. Geraghty, newly elected President of the Baltimore City Medical Society; and Dr. and Mrs. Homer U. Todd, Sr. Mrs. Todd is the President of the Woman's Auxiliary to the Medical and Chirurgical Faculty of Maryland.

Coming Meetings

Orthopedic Section, B.C.M.S.
Friday, March 1, 1957 Evening Philadelphia, Pa.

Baltimore City Medical Society
Friday, March 8, 1957 8:30 P.M. 1211 Cathedral Street

Woman's Auxiliary to the Baltimore City Medical Society
Friday March 8, 1957 9:00 P.M. Emerson Hotel; dance and midnight supper

Pediatric Section, B.C.M.S.
Tuesday, March 12, 1957 8:30 P.M. 1211 Cathedral Street

Cancer Section, B.C.M.S.
Wednesday, March 13, 1957 6:30 P.M. Dinner Meeting, Baltimore City Hospital

General Practice Section, B.C.M.S.
Thursday, March 21, 1957 9:30 P.M. 1211 Cathedral Street

Committee for the Study of Pelvic Cancer
Thursday, March 21, 1957 5:00 P.M. Mercy Hospital

Dermatological Section, B.C.M.S.
Monday, March 25, 1957 6:00 P.M. Dinner Meeting, University Club

Joint Committee on Maternal Mortality, City Health Dept. and B.C.M.S.
Thursday, March 28, 1957 4:00 P.M. 1211 Cathedral Street

Annual Meeting Medical and Chirurgical Faculty
May 1, 2, 3, 1957 ——— 1211 Cathedral Street

All meetings are held in the Medical and Chirurgical Faculty Building, 1211 Cathedral Street, Baltimore, Md., unless otherwise designated.

ANNUAL LECTURE

The annual lecture of the Phi Delta Epsilon Fraternity of Baltimore will be given at 8:15 P.M. on March 22, in Gordon Wilson Hall of the University Hospital, University of Maryland Medical School. The speaker will be Dr. Paul Hoch, Commissioner of Mental Hygiene of the State of New York. The title of Dr. Hoch's paper will be "The Use and Abuse of Tranquillizing Drugs."

The paper will be discussed by Dr. Jerome Frank, Professor of Psychiatry, Johns Hopkins University, and Dr. John C. Krantz, Jr., Professor of Pharmacology, University of Maryland Medical School.

Attention

Annual Meeting Dates

MEDICAL AND CHIRURGICAL FACULTY

MAY 1, 2, 3, 1957

Business Meetings—Wednesday and Friday mornings, May 1 and 3, 1957.

Scientific Sessions—Wednesday afternoon, May 1; all day Thursday, May 2; and Friday afternoon, May 3, 1957.

Woman's Auxiliary Luncheon—Wednesday, May 1, 1957.

Medicolegal Symposium—Wednesday evening, May 1, 1957.

Round Table Luncheon—Thursday, May 2, 1957.

Presidential Dinner and Meeting—Thursday evening, May 2, 1957.

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Be sure to attend the various scientific sessions and functions during the coming Annual Meeting. A most interesting program is being arranged by your Committee on Scientific Work and Arrangements, and there will be many excellent local and out-of-town speakers. Among the out-of-town doctors who will participate are: Dr. Dwight H. Murray, President of the American Medical Association; Dr. Samuel H. Proger, Professor of Medicine at Tufts University School of Medicine; Dr. George E. Schreiner, Assistant Professor of Medicine and Director of the Renal Clinic at Georgetown University Medical Center; and Dr. Fredrick J. Stare of the Department of Nutrition at the Harvard University School of Public Health.